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Original Communications

THE EAR COMPLICATIONS OF SCARLET FEVER

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ONE of the most frequent and serious complications of scarlet fever is that which pertains to the ears. The number of such complications is exceeded only by cervical lymphadenitis. Variations in the incidence of otitis media as a complication of scarlet fever may be influenced by many factors, including climatic conditions, age, virulence of the infecting organism, and the susceptibility of any given population.

Usually, the pediatrician, or the general practitioner, is the first to see and diagnose the complications of scarlet fever. Although, in many instances, otitis media may be treated by physicians other than otologists, the complications of middle ear suppuration usually are placed under the care of the latter. Consequently, effective cooperation between the otolaryngologist and pediatrician or general physician is essential to prevent or treat properly serious complications due to otitis media in scarlet fever patients. For this reason, it is the opinion of the authors that the importance and seriousness of otitis media as a complication of scarlet fever should be appreciated more fully by the medical profession.

In order to secure more definite information pertaining to this subject, a study was made of the ear complications among 3,564 scarlet fever patients treated at the Chicago Municipal Contagious Disease Hospital during the period of July 1, 1934 to June 30, 1935.

In Table I are shown the number and percentage of patients who developed otitis media, the character of the inflammation, and its unilateral or bilateral occurrence.

Since it was suspected that the incidence of otitis media might be unduly high in the above group of patients, a number of the more im-

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TABLE I

THE INCIDENCE OF OTITIS MEDIA AMONG 3,564 SCARLET FEVER PATIENTS

NATURE OF THE EAR INVOLVEMENT	UNILATERAL		BILATERAL		TOTAL	
	NO.	PER CENT*	NO.	PER CENT	NO.	PER CENT
Catarrhal	23	0.64	6	0.16	29	0.80
Purulent	324	9.09	152	4.26	476	13.35
Catarrhal + purulent†	---	----	---	----	5	0.10
Total	347	9.73	158	4.43	510	14.30

*Percentage calculated as follows: $\frac{\text{No. pt. with otitis media}}{3,564} \times 100$

†One ear with catarrhal, the other with purulent form of otitis media. These cases have been excluded from further analysis in this paper.

portant contributions to the literature were reviewed for purposes of comparison. This information is summarized in Table II.

TABLE II

INCIDENCE OF PURULENT OTITIS MEDIA AMONG SCARLET FEVER PATIENTS

AUTHORS	NUMBER OF SCARLET FEVER PATIENTS	NUMBER OF CASES OF PURULENT OTITIS MEDIA	PERCENTAGE INCIDENCE OF PURULENT OTITIS MEDIA	SOURCE OF CASES QUOTED BY VARIOUS AUTHORS
Ross, E. L.[1]	80,144	9,378	11.7*	Review of the reports of 12 different authors quoted in his paper.
Ross, E. L.[1]	2,595	370	14.2	Durand Contagious Disease Hospital, Chicago, 1912-1922.
Williams, H. J.[2]	29,298	2,898	9.9	Philadelphia Contagious Disease Hospital, 1922-1934.
Harries, E. H. R., and Gillespie, F. B.[3]	3,864	280	7.6	Birmingham (England) City Hospital, 1921-22.
Hunter, Wm., quoted by Harries and Gillespie[3]	648	68	10.6	London Fever Hospital, 1904-1907.
Schmidt, V.[4]	2,757	296	10.7	Epidemic of scarlet fever in Copenhagen in 1934.
Gordon, J. E.[5]	10,666	1,182	11.08	Herman Kiefer Hospital, Detroit, Michigan.
Gardiner, W. T.[6]	3,728	300	8.04	Edinburgh City Hospital for Infectious Diseases, 1920-1922.
Lefler, A. B.[7]	473	58	12.25	Los Angeles General Hospital.
Strachan, J. G.[8]	589	98	16.60	Isolation Hospital, Toronto.
Armstrong, E. K., quoted by Friedberg, S. A.[9]	100	23	23.00	Cook County Contagious Disease Hospital.
Total	134,862	14,951	11.08	

*According to the different reports, the percentage incidence of purulent otitis media varied from 3.75 to 25.0.

It is noteworthy that, according to the report selected, the incidence of suppurative otitis media varied from a percentage as low as 3.75

to one as high as 25. In similar fashion, Kolmer and Schamberg[10] quote figures ranging from 4.5 to 75 per cent; and Schlossmann and Hottinger[11] report corresponding rates of 15 to 50.

The tendency of scarlet fever otitis to involve the mastoid cells in a destructive process is very aptly described by Schlossmann and Hottinger:[11] "The scarlet otitis has a tendency to affect the antrum, the cells of the mastoid process and the bone, in spite of profuse drainage of the pus from the opening of the ear drum." In Table III is recorded the fact that 45.16 per cent of 476 cases of purulent otitis media developed mastoiditis. The incidence of this complication was significantly higher among the fatal than among the recovered cases of suppurative otitis media.

TABLE III

FREQUENCY OF MASTOIDITIS AS A COMPLICATION AMONG 476 PATIENTS WITH PURULENT OTITIS MEDIA

	RECOVERED CASES WITH PURULENT OTITIS MEDIA	FATAL CASES WITH PURULENT OTITIS MEDIA	ALL CASES WITH PURULENT OTITIS MEDIA
Number of patients with purulent otitis media	439	37	476
Number of cases of otitis media complicated by mastoiditis	192	23	215
Percentage of cases of purulent otitis media complicated by mastoiditis	43.73	62.16	45.16

Of 215 cases of mastoiditis, involvement was unilateral in 167 and bilateral in 48 cases.

A total of 124 cases, or 57.6 per cent of those with clinical signs or symptoms of mastoiditis, required surgical treatment. The remainder were given medical therapy alone.

In Table IV are shown the number and percentage of cases of purulent otitis media which required either unilateral or bilateral mastoidectomy.

TABLE IV

NUMBER AND PERCENTAGE OF CASES OF PURULENT OTITIS MEDIA WHICH REQUIRED MASTOID OPERATIONS

TOTAL CASES OF PURULENT OTITIS MEDIA	UNILATERAL MASTOIDECTOMY		BILATERAL MASTOIDECTOMY		TOTAL	
	NO.	PER CENT*	NO.	PER CENT	NO.	PER CENT
476	99	20.80	25	5.25	124	26.05

*Calculated as follows: $\frac{\text{Cases given mastoidectomy}}{476} \times 100$

It is of interest to compare the incidence of surgical mastoiditis noted in our series of cases with the findings of other writers. During the 1934 epidemic of scarlet fever in Copenhagen, Viggo Schmidt[4] reported a 44.6 per cent incidence of surgical mastoiditis among 157 cases of scarlet fever otitis treated by the usual conservative means. In another

group of 139 patients with draining ears, seen during the same period but treated by alcohol syringing through the external auditory meatus, the mastoidectomy rate was only 5.8 per cent. Williams[2] reported that 12.5 per cent of 363 cases of purulent otitis media, seen at the Philadelphia Contagious Disease Hospital from 1922 to 1934, were submitted to the mastoidectomy operation. Lefler,[7] quoting observations at the Los Angeles General Hospital, noted a mastoidectomy rate of only 3.4 per cent for a group of 58 cases with ear involvement. In summary, the mastoidectomy rate observed in our series is high if compared to those reported by Lefler,[7] Williams,[2] and Viggo Schmidt,[4*] but low if contrasted with the incidence of surgical mastoiditis among the group of Schmidt[4] treated during essentially the same time and by the same conservative technique employed in our cases.

To what degree is the patient with scarlet fever likely to develop mastoiditis? Analysis of Table V reveals the interesting fact that 6.02 per cent of all cases of scarlet fever in our series suffered from this complication. The inflammatory involvement of the mastoid process was unilateral in 4.68 and bilateral in 1.34 per cent of the scarlet fever patients.

TABLE V

INCIDENCE OF MASTOIDITIS AMONG 3,564 CASES OF SCARLET FEVER*

UNILATERAL MASTOIDITIS		BILATERAL MASTOIDITIS		ALL CASES OF MASTOIDITIS	
NO.	PER CENT†	NO.	PER CENT	NO.	PER CENT
167	4.68	48	1.34	215	6.02

*Includes cases detected during life or at necropsy.

†Calculated as follows: $\frac{\text{No. cases of mastoiditis}}{3{,}564} \times 100$

As already noted, not all cases of mastoiditis appeared to require a mastoid operation. Although 6.02 per cent of all scarlet fever cases developed mastoiditis, only 3.47 per cent of all patients were submitted to mastoidectomy. This operation was unilateral in 2.77 and bilateral in 0.70 per cent of all the cases of scarlet fever. These data are presented in Table VI.

TABLE VI

NUMBER AND PERCENTAGE OF CASES OF SCARLET FEVER WHICH REQUIRED MASTOID OPERATIONS

CASES OF SCARLET FEVER	UNILATERAL MASTOIDECTOMY		BILATERAL MASTOIDECTOMY		TOTAL	
	NO.	PER CENT*	NO.	PER CENT	NO.	PER CENT
3,564	99	2.77	25	0.70	124	3.47

*Calculated as follows: $\frac{\text{Cases given mastoidectomy}}{3{,}564} \times 100$

The mastoidectomy rate recorded in Table VI is high if compared with the corresponding figures of 1.24 per cent indicated by the report

*Group treated with alcohol syringing of external auditory canal.

of Williams[2] and of 0.72 per cent based on the data submitted by Viggo Schmidt[4] for the series given the benefit of alcohol syringing. On the other hand, it is low if contrasted with the rate of 4.24 per cent calculated from the figures given by Schmidt for the group treated by the usual conservative means.

Table VII shows the fatality rates for 215 cases of mastoiditis which received either operative or nonsurgical treatment.

TABLE VII

MORTALITY RATES AMONG 215 CASES OF MASTOIDITIS FOLLOWING OPERATIVE AND NONOPERATIVE TREATMENT

TREATMENT OF MASTOIDITIS	RECOVERIES		FATALITIES		TOTAL		PER CENT MORTALITY WITH AND WITHOUT OPERATION
	NO.	PER CENT OF RECOVERED CASES	NO.	PER CENT OF FATAL CASES	NO.	PER CENT OF ALL CASES	
Operative	106	55.21	18	78.70	124	57.68	14.51
Nonoperative	86	44.79	5	21.30	91	42.32	5.49
Total	192	100.00	23	100.00	215	100.00	10.67

While it might appear that the chances of recovery were reduced as a result of operative intervention, in reality, the group given only medical treatment consisted of cases which were far less severe, in which clinical signs of mastoid cell invasion were relatively mild. The decision concerning operative intervention was reached only after careful consideration of each individual case, in which recognized otologists acted as consultants. Therefore, it is significant that only 55.21 per cent of the recovered cases of mastoiditis were considered in need of operative therapy, in contrast with 78.70 per cent of the fatal cases.

As one might readily anticipate, bilateral surgical mastoiditis, as contrasted with unilateral involvement, definitely increases the hazards in the pathway of recovery. This is well illustrated in the fatality rates shown in Table VIII.

TABLE VIII

FATALITY RATES FOR CASES TREATED BY UNILATERAL OR BILATERAL MASTOIDECTOMY OPERATION

EXTENT OF THE OPERATION	RECOVERIES	FATALITIES	TOTAL	PER CENT MORTALITY
Unilateral mastoidectomy	88	11	99	11.11
Bilateral mastoidectomy	18	7	25	28.00
Total	106	18	124	14.51

Suppurative otitis media, occurring during the acute stage or convalescence in the scarlet fever patient, may endanger either the hearing or life of the individual. Usually, loss of life following ear involvement may be attributed to the extension of bacterial infection beyond the confines of the mastoid cells into structures in the immediate vicinity, or to

the development of septicemia. Table IX summarizes the more salient complications observed among the 215 cases of mastoiditis described in Table III.

TABLE IX

COMPLICATIONS AMONG 215 CASES OF MASTOIDITIS OCCURRING IN 3,564 CASES OF SCARLET FEVER

COMPLICATIONS OF MASTOIDITIS	FREQUENCY GIVEN COMPLICATIONS WERE OBSERVED		
	RECOVERIES	FATALITIES	TOTAL
Septicemia	15	19	34
Lateral sinus thrombosis	12	7	19
Jugular bulb thrombosis	3	7	10
Meningitis	-	4*	4*
Perisinus abscess	6	4	10
Extradural abscess	1	3	4
Cerebellar abscess	-	2	2
Endocarditis	-	2	2

*Localized purulent leptomeningitis—noted in 2 cases.
Diffuse, streptococcus meningitis—noted in 2 cases.

While the figures are self-explanatory, certain facts seem worthy of special mention. The high incidence of septicemia, lateral sinus or jugular bulb thrombosis, and perisinus abscess emphasizes the need of careful search for their presence in the septic scarlet fever patient with suppurative otitis media. The high recovery rate, in response to heroic medical and surgical therapy, warrants the most painstaking efforts to detect the presence of these otherwise fatal complications.[12]

It is of interest to note the week of the disease in which suppurative otitis media most frequently develops. This is indicated in Table X.

TABLE X

WEEK OF ONSET OF PURULENT OTITIS MEDIA*

WEEK OF ONSET OF THE OTITIS	RECOVERED CASES	FATAL CASES	ALL CASES	PERCENTILE DISTRIBUTION OF CASES
1	157	11	168	35.20
2	122	11	133	27.90
3	75	6	81	17.00
4	39	5	44	9.30
5	24	1	25	5.25
6	3	1	4	0.87
7	6	-	6	1.26
8	3	1	4	0.87
9	1	-	1	0.21
10	1	-	1	0.21
12 and later†	4	-	4	0.87
Unknown	4	1	5	1.05
Total	439	37	476	99.99

*Included in the total are a negligible number of patients who had a purulent otitis media at the time of admission to the hospital.

†In 3 instances, suppurative otitis media developed between three and one-half and seven months after the onset of scarlet fever.

Analysis of Table X reveals that the greatest frequency was observed during the first week of scarlet fever. A gradual decline in the inci-

dence of otitis media appeared in the second and third weeks. Thereafter, a sharp drop in this complication took place. It is a fact worthy of note that approximately 95 per cent of all cases of suppurative otitis media in this series appeared within the first six weeks after the onset of the disease. From a prognostic standpoint, however, it is well to bear in mind the fact that purulent otitis media may occur as late as seven months after the onset of scarlet fever. Schlossmann and Hottinger[11] stress the importance of this point: "Ear clinics and polyclinics are frequently sought by scarlet fever convalescents, who do not connect the ear trouble with their recent recovery from scarlet fever, and therefore are not aware of their infectious capacity and give insufficient information about the primary cause. They are the chief sources of relatively frequent infection of other patients in the waiting-rooms of ear clinics. . . . This danger from ear clinics is expressed also in the statistics of the infectious disease clinic of Düsseldorf; the small ear-nose-throat clinic was much more frequently disrupted than the other clinics, inclusive of the surgical clinic, by the transfer of scarlet fever patients to the infectious disease ward. . . . We have repeatedly had the experience that an apparently well child was discharged and in the seventh or eighth week at home he contracted otitis and then infected his brothers and sisters with scarlet fever."

It is a matter of frequent observation that scarlet fever is particularly common under the age of ten years, and that ear complications and fatality rates are highest during this age period.[2, 3] Table XI clearly confirms the validity of such an assertion.

TABLE XI

INCIDENCE OF PURULENT OTITIS MEDIA ACCORDING TO AGE, AND ITS IMPORTANCE AS A CAUSE OF DEATH

AGE IN YEARS	NO. OF SCARLET FEVER PATIENTS	CASES OF PURULENT OTITIS MEDIA	PERCENTAGE INCIDENCE OF PURULENT OTITIS MEDIA	DEATHS FROM PURULENT OTITIS MEDIA	FATALITY PER CENT CAUSED BY THE PURULENT OTITIS MEDIA	DEATHS FROM ALL OTHER CAUSES	FATALITY PER CENT DUE TO ALL OTHER CAUSES
1- 5	1,067	219	20.5	22	2.0	20	1.8
6-10	1,396	189	13.5	12	0.8	9	0.6
11-15	512	38	7.4	1	0.1	2	0.4
16-20	164	10	6.0	--	--	1	0.6
21 and above	412	20	4.8	2	0.4	6	1.4
Not stated	13	---	---	--	--	--	--
Total	3,564	476	13.3	37	1.0	38	1.0

A perusal of Table XI affords convincing evidence that more deaths are attributable to purulent otitis media than to any other single complication. Moreover, it is obvious that the fatality rate of scarlet fever attributable to purulent otitis media is equivalent to that occasioned by

all other complications. Harries and Gillespie[3] emphasize the fact that the greatest mortality from scarlet fever occurs up to the age of five years, and that these young children die not from toxicity, but from the septic type of the disease, with otitis media as one of the outstanding complications secondary to overwhelming infection of the nasopharynx.

COMMENTS

We have attempted to emphasize the vital importance of ear complications in the prognosis of scarlet fever. In addition, it has been our purpose to present figures illustrative of the high percentage of fatalities directly traceable to purulent otitis media. The frequency with which mastoiditis, and its sequelae, follow otitis media has been cited.

With the knowledge at hand, consideration properly should be given to the best means of reducing both the incidence and risk of purulent otitis media.

While it is conceded that the prevention of scarlet fever, by means of active immunization, would be a most important step toward a reduction of the incidence of ear complications, the controversial status of this procedure precludes definite remarks or recommendations.

There seems to be no doubt that the selection of therapeutic measures in the acute stage of scarlet fever may have a very distinct influence upon the incidence of otitis media. General supportive measures, including blood transfusions, parenteral fluids, adequate diet, and effective sedative therapy, would appear to render the patients more capable of resisting middle ear and mastoid cell invasion by the offending bacterial agents. Maintenance of unobstructed nasal chambers, by means of the topical application of ephedrine or allied vasoconstrictors, supplemented by cautious nasal suction, is essential to prevent mechanical spread of septic material from the nasopharynx to the middle ear by way of the eustachian tubes. However, it is to be stressed that irrigations of the nose or throat with antiseptic solutions are to be avoided. The throat should be kept clean by care of the nose in the manner already indicated. The administration of adequate amounts of fluids of a bland nature by the oral route is the most desirable method of maintaining cleanliness of the mouth and nasopharynx. In our opinion, gargles are definitely contraindicated in the early acute stage of scarlet fever, because of the danger of facilitating spread of septic material into the middle ear. Furthermore, gargling by small children is neither feasible nor logical.

It is our belief that all uncomplicated cases of scarlet fever should be separated from those with purulent otitis media or other complications which might facilitate reinfection and the appearance of aural inflammation. Such a point of view is supported by Harries and Gillespie[3] and Gardiner,[6] who recommend separate wards for cases with otitis media, together with barrier nursing technique.

In similar fashion, protection against cross-infection from other contagious diseases, particularly measles, is essential. For, occasionally a mild uncomplicated case of scarlet fever assumes a serious aspect because of otitic involvement following cross-infection by a measles patient.

While prophylactic measures, outlined above, may contribute to a reduction of the incidence of purulent otitis media, this complication may appear nevertheless and require treatment. Unfortunately, there is considerable difference of opinion concerning proper methods for the treatment of acute suppurative otitis media.

We believe that undue resort to paracentesis in the case of scarlet fever is to be condemned. In respect to early paracentesis, we agree with the teaching of Kopetzky[13]: "As a result of long observation, it has become evident that to incise the drum too early in the course of the development of an acute suppuration of the middle ear is to add a factor toward the promotion, rather than toward the retardation, of the middle ear infection." However, in the presence of a bulging membrana tympani, particularly associated with aural or mastoid pain or tenderness, with or without fever, paracentesis seems to be a justifiable procedure. Nevertheless, when such surgical intervention does become necessary, the operation should be undertaken only by an experienced otologist or by a physician who has had an extensive practice in this procedure. The importance of having a competent otologic consultation at the earliest appearance of suspicious symptoms should never be minimized. Proper treatment at such a time may curtail future serious complications. Such a point of view is confirmed by the reports of both Gardiner[5] and Lefler.[7] For satisfactory accomplishment of the paracentesis, a light gas anesthesia is of considerable value. Strict asepsis is of the utmost importance; and this implies that the entire ear canal and the membrana tympani are to be thoroughly cleansed before the operation is undertaken.

Concerning repeated paracentesis, we agree with the statement of Williams[2]: "The writer would like to state here that he does not favor repeated incisions of the eardrums, as he feels that the bulging of the tympanic membrane, which invites repeated incisions, usually is due to the enormous swelling and edema of the mucosa of the middle ear and not due to localized pus, and repeated incision is often not only valueless, but that it inflicts useless trauma on the tympanic membrane and middle ear structures." However, we recognize that there are many occasions upon which second and third paracenteses may be justified, as shown by the establishment of more adequate drainage after their performance.

Divergent teachings prevail concerning the irrigation of draining ears. For the past eighteen years, such irrigations have not been permitted at the Chicago Municipal Contagious Disease Hospital. However, in view of the favorable report of Schmidt,[4] already quoted, the possible

beneficial action of alcohol irrigations must receive careful consideration. Nevertheless, aqueous solutions for purposes of irrigation are mentioned only to be condemned. In our opinion, the ultimate outcomes of ear complications are often adversely influenced by the secondary infections entailed in the process of treatment. Consequently, independent of the selection of dry or moist cleansing of the external auditory canal, a strict aseptic technique is absolutely essential.

We have observed that the presence of adenoids and enlarged tonsils is a very important factor in the development of otitis media in scarlet fever patients. For some time it has been the opinion of one of us (A. L. H.) that removal of adenoids and enlarged tonsils before children entered school would result in a lower incidence of ear complications among those who later contracted scarlet fever. This viewpoint is supported by the excellent results noted by Gardiner[5] when adenoids, and tonsils if necessary, were removed in the course of otorrhea. This operation, according to his report, was associated with a 23.5 per cent decrease in the average duration of the aural discharge. In addition, after such surgical intervention, a high percentage of the primary otorrheas had subsided within seven days after operation and remained dry while under hospital observation. All cases of primary otorrhea left the hospital with dry ears. No adverse sequelae were noted despite the fact that the operations were performed in a fever hospital. Gardiner advised removal of adenoids at the time of the first paracentesis, independent of the duration of the scarlet fever, in order to avoid the necessity of repeating the administration of a second general anesthesia. Williams[2] recommended removal of the tonsils and adenoids after the aural discharge had persisted for about three weeks. In summary, a review of the above facts and recommendations suggests that the patient with otorrhea, before the onset of mastoid involvement, should be given the benefit of adenoidectomy lest mastoid cell invasion be incriminated as the cause of the prolonged aural discharge. Furthermore, if mastoidectomy is performed, it would seem desirable to remove the adenoids at the time of this operation.

We have noted repeatedly that mastoiditis, following otitis media in scarlet fever patients, may be insidious in onset. We are in accord with the teaching of Gardiner[5] to the effect that the absence of typical signs and symptoms does not rule out the presence of mastoiditis. We have frequently observed the type of mastoiditis described by Gardiner,[5] appearing in the fourth or fifth week of aural discharge, without pain, tenderness, or fever, with marked mastoid cell suppuration, often accompanied by subperiosteal abscess formation or spread of purulent material to the wall or interior of the lateral sinus. For this reason, we wish to emphasize the necessity of anticipating mastoid involvement before serious systemic or intracranial complications supervene.

SUMMARY

1. A study of the ear complications among 3,564 scarlet fever patients is presented.

2. The subject is analyzed and tables given which show the following:

(a) The incidence of otitis media among 3,564 scarlet fever patients.

(b) The frequency of otitis media among 134,862 cases of scarlet fever collected from the more important contributions to the literature.

(c) Incidence of mastoiditis as a complication among 476 patients with purulent otitis media.

(d) Number and percentage of cases of purulent otitis media which required mastoid operations.

(e) Incidence of mastoiditis among 3,564 cases of scarlet fever.

(f) Number and percentage of cases of scarlet fever which required mastoid operations.

(g) Mortality rates among 215 cases of mastoiditis following operative and nonoperative treatment.

(h) Fatality rates for cases treated by unilateral or bilateral mastoidectomy operation.

(i) Complications among 215 cases of mastoiditis occurring in 3,564 cases of scarlet fever.

(j) Week of onset of purulent otitis media.

(k) Incidence of purulent otitis media according to age, and its importance as a cause of death.

3. Extracts from the literature pertaining to this subject are discussed.

4. Reference is made to different methods employed in the treatment and prevention of suppurative otitis media.

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THE CONSERVATIVE MANAGEMENT OF APPENDICEAL PERITONITIS IN CHILDREN

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INTRODUCTION

A SIGNIFICANT reduction in the high mortality of peritonitis secondary to appendicitis in children, attained by deferring surgical intervention until the acute process has subsided, deserves consideration. This conservative trend has already received wide recognition in treatment of diseases such as acute salpingitis and cholecystitis.

There is universal satisfaction with the therapeutic results in acute appendicitis. Early diagnosis and prompt surgery, employed before the infectious process has extended beyond the appendix, has brought about this result. The problem, however, is presented by the cases in which extra-appendiceal extension has occurred and peritonitis is present.

Keyes[1] reporting from Barnes Hospital, St. Louis, found 50.3 per cent and Finney[2] analyzing 1,807 cases found 37.5 per cent with extension on admission. The mortality rate in those cases confined to the appendix was 1.4 per cent. On the contrary a mortality of 10.1 per cent was found in 678 cases of ruptured appendicitis. In no group is the problem more acute than in children. Davis and his associates[3] state that the high mortality in young children is due to the high incidence of appendicitis in the acute form in this group and especially the occurrence of rupture. They reported 402 cases in children ten years and under, 75.4 per cent of which were acute. There were 43 deaths in the entire group, a mortality of 10.69 per cent. Assuming that these deaths occurred in the acute group, the mortality would be 14 per cent. In the ruptured group the mortality was not given.

Coller and Potter[4] state that the younger the child, the greater will be the mortality in any form of treatment. The difference between the child and the adult has been attributed to late diagnosis, almost universal purging, the anatomic and physiologic characteristics peculiar to the child, such as the omentum, which is much less developed than in adults.

The principles of the conservative treatment and the basis for its use have been well reviewed by Ochsner[5] in his recent paper. In brief he states that the peritoneum, following bacterial trauma, becomes inflamed and forms fibrinous adhesions, which along with the omentum will wall off the inflammatory process and prevent dissemination of the offending

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organisms. The danger of extension of the infectious process is less if the protective adhesions are not broken down as may occur during removal of the appendix.

METHOD OF STUDY

It has been the policy of the pediatric and surgical departments of this hospital to treat all cases of acute appendicitis in children in which there is evidence of perforation or extension conservatively. All cases of acute appendicitis in children under sixteen years of age seen in this hospital between January 1934 and April 1937 have been studied. There have been 241 cases, 110 of which were considered to have good evidence of extra-appendiceal extension when first seen. All cases of advanced peritonitis have been included in the conservative group unless proved not to be of appendiceal origin.

During the period of this study there have been no control cases as a clinical study of this nature does not permit selection of comparable cases. However, the mortality figures reported from this hospital on a group of children, all operated upon prior to this period, have been summarized.

The indications for the use of the conservative treatment in children have not heretofore been well established. From our observations of the conservative group we have attempted to evaluate the indications which should be of assistance in deciding when operative interference or the conservative management should be employed.

The clinical course has been studied. The surgical and pathologic findings have been analyzed in 94 patients, all of whom have had deferred appendectomies. The conservative treatment as carried out here is outlined and several cases are presented to illustrate the typical as well as the atypical record. The fatal cases are presented in chart form; the complications and mortality are discussed.

THE CONSERVATIVE TREATMENT

The conservative treatment as first outlined by Dr. A. J. Ochsner in 1892, is in principle what is used in this hospital today, modified by the use of continuous gastroduodenal siphonage instituted by Dr. Owen H. Wangensteen.

Success in the application of the conservative treatment depends on an understanding of the basic principles involved, the main component of which is rest. The gastrointestinal tract is almost completely relieved of activity by the use of the gastroduodenal siphonage which continuously removes gas and fluid secreted by the stomach, intestine, as well as the accessory secretions such as bile and pancreatic juices.

A diagram of the siphonage system is presented in Fig. 1. At the onset the upper bottle is filled with water except for 400 c.c. and the lower bottle is empty except for 400 c.c. in the bottom to cover the tube. The amount of gas taken off is read directly on the upper bottle, and

the amount of fluid removed is shown on the lower bottle. Multiple perforations are essential on the distal end of the nasal tube to permit gastric and duodenal siphonage. It is also important to make sure that the tube from the patient is connected with the long piece of glass tubing in the upper bottle.

The child is placed flat in bed. The semi-Fowler's position is not maintained well by children, and often necessitates more manipulation

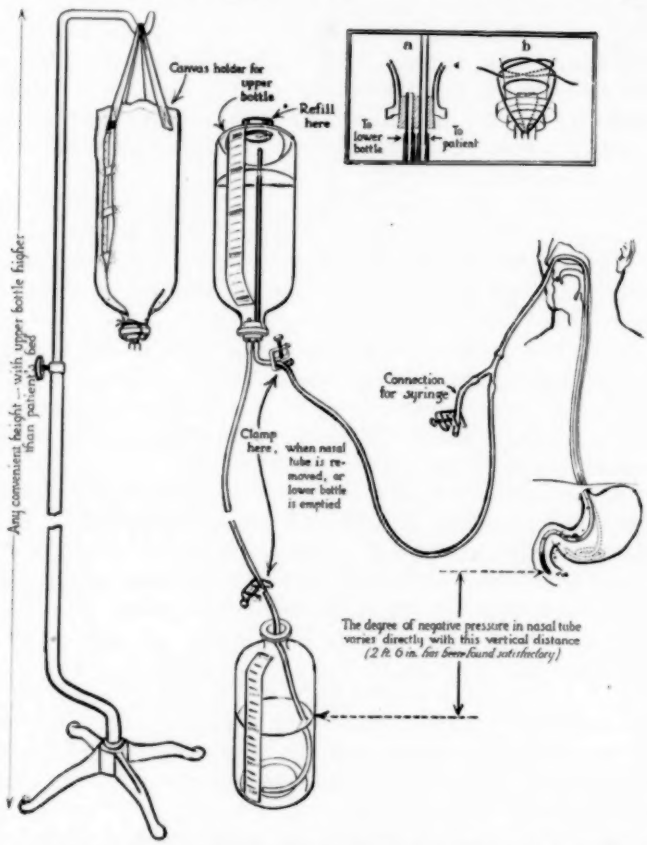

Canvas holder for upper bottle
Refill here
a
b
To lower bottle
To patient
Any convenient height — with upper bottle higher than patient's bed
Connection for syringe
Clamp here, when nasal tube is removed, or lower bottle is emptied
The degree of negative pressure in nasal tube varies directly with this vertical distance
(2 ft. 6 in. has been found satisfactory)

Fig. 1.—A diagram of the gastroduodenal siphonage apparatus used in nearly all the cases of appendiceal peritonitis.

than if the patient is allowed to remain flat in bed. The passage of the tube offers little difficulty. The patient is allowed to swallow water as the tube is being passed. Small amounts of clear fluids are allowed as desired by mouth at all times as they are immediately withdrawn by the tube. The patient is kept on the right side and the tube passed in 2 or 3 inches every two hours for the first twelve hours in order to facilitate its passage into the duodenum. The progress of the tube may be checked by

portable x-ray as necessary (see Fig. 4). The nature of the return will frequently indicate when it is in the duodenum.

Hot applications are applied to the abdomen in the form of stoops. Sedatives are administered for control of activity, pain, and in order to depress the respiratory rate slightly. Codeine and phenobarbital are used in suitable doses. Fluids are administered by vein and hypodermoclysis. No fluids are given by rectum and no enemas are given. Physiologic saline with 5 per cent dextrose added is given by intravenous drip, approximately 90 to 100 c.c. per kilogram of body weight is given daily as long as continuous siphonage is maintained. More fluids may be required during the hot summer months to maintain proper fluid and electrolyte balances, or if there has been a previous excess loss of fluid from vomiting or diarrhea.

The response to treatment is noted in less than forty-eight hours in most cases by a decline in the temperature and pulse. The general appearance of the patient is improved. Siphonage relieves the pain and distention markedly and vomiting is rare following its use. The indications for the use of suction are pain, vomiting, distention, and intestinal activity, all of which are favorably affected by its application. The system is allowed to provide continuous suction until the temperature reaches normal, usually five to six days, but may be continued for as long as two weeks.

The formation of a mass is discussed under "Physical Findings." The patients are kept in the hospital until they are taking an adequate soft diet and until the mass has disappeared. The average duration of hospitalization has been 18.7 days. On discharge, instructions are given to limit activity at home, and a soft diet is prescribed.

OBSERVATIONS

All cases of appendicitis in children observed in the University of Minnesota Hospital from January 1934 to April 1937 are presented in Table I. In the group of acute appendicitis without extension operated

TABLE I

SUMMMARY OF ALL CASES BY YEAR WITH DIVISION OF CASES ACCORDING TO DIAGNOSIS AND TREATMENT. THE MORTALITY IS SHOWN IN EACH GROUP

YEAR	ACUTE APPENDICITIS: IMMEDIATE APPENDECTOMY	DEATHS	APPENDICEAL PERITONITIS: CONSERVATIVE TREATMENT	DEATHS	PATIENTS TREATED CONSERVATIVELY: DEFERRED APPENDECTOMY	PATIENTS TREATED CONSERVATIVELY: FAILURE TO RETURN	PER CENT TREATED CONSERVATIVELY
1934	50	1	32	2	29	1	39
1935	36	0	29	2	25	2	45
1936	34	0	34	1	30	3*	50
1937	11	0	15	0	10	5*	57
						3	
Total	131	1	110	5	94	8*	45

*Cases which have appointments to return for interval appendectomy.

upon immediately there was one death. The child became extremely cyanotic and died in a convulsion on the operating table. Death was attributed to anesthesia. In the group complicated by extra-appendiceal extension and treated conservatively there were five deaths. Attention is directed to the fact that these two groups are in no way comparable. Eliminating the single death due to anesthesia, there have been no fatalities following immediate or deferred surgery. This absence of surgical deaths in all operated cases speaks forcefully for the conservative management of the more advanced cases. The increasing percentage of cases treated conservatively indicates a definite trend toward the further adoption of the conservative management. Failures to return for deferred appendectomy have been less than 5 per cent.

Indications for Conservative Management

Age.—In Fig. 2 the entire group of 241 cases is plotted according to age. It will be seen that the incidence of appendicitis mounts steadily from the first through the fifteenth year. When the complicated cases are separated from the uncomplicated and plotted according to age, two curves are produced which are not only unlike each other but differ from the incidence curve. It will be seen that out of 38 cases seven years and under, 31 or 81.6 per cent were complicated. Above seven years of age the number of cases in which the diagnosis of appendicitis was made before extension had occurred rapidly increased with succeeding years. From the seventh through the fifteenth year only 39 per cent were complicated. In those of fourteen and fifteen years only 28 per cent were complicated.

In the group seven years or under in which the incidence of extension is so high, and in which a high mortality is recorded, there was but one death in 31 cases treated conservatively, i.e., a mortality of 3 per cent.

Duration.—Frequently the statement is made that any case of acute appendicitis under forty-eight hours' duration should be operated upon at once. On the chart (Fig. 3) including all cases treated conservatively it will be noted that 53 cases were forty-eight hours or less in duration; the largest group of cases was observed in the period between thirty-six and forty-eight hours. There were 33 cases of three, four, and five days' duration, the remaining 24 cases being widely scattered. There were no deaths in the extended group, all fatalities occurring in patients with histories from thirty-nine to ninety-six hours' duration. We have come to consider the duration as only one factor determining the course of treatment. The progress of the disease is probably of the greatest consequence; we might better speak of uncomplicated and complicated appendicitis rather than early and late.

Temperature and Pulse.—On admission these findings were found to be of considerable assistance in deciding the question of operative or

conservative treatment. The average temperature and pulse of all cases of complicated appendicitis treated conservatively is shown in Table II. The average temperature on admission was 101.7° F.; the pulse, 119 per minute. In the typical case the temperature is found to be around

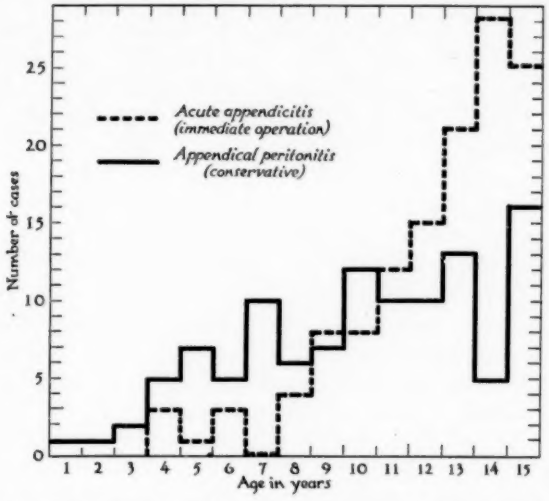


Fig. 2.—A chart showing the age incidence of the uncomplicated operated group as contrasted with the cases of appendiceal peritonitis treated conservatively.

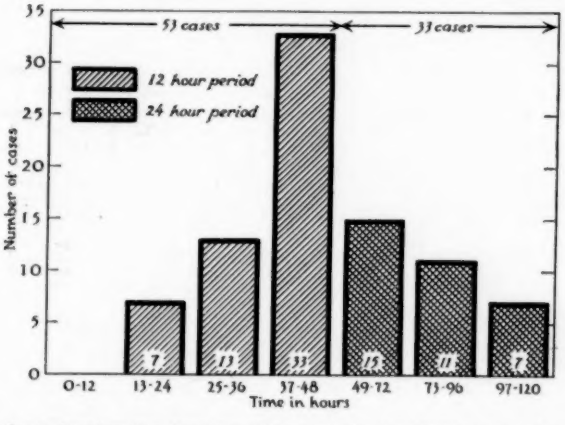


Fig. 3.—A chart showing the duration of present illness of the group classed as appendiceal peritonitis. In 24 cases the duration was over five days.

102° F. to 103° F. with a rapid pulse of 130 to 150 per minute. However, it will be seen from the general averages that the figures are well above those ordinarily seen in cases of uncomplicated appendicitis. Many cases coming in late, that is, after five days, tend to lower the

TABLE II

SUMMARY OF LABORATORY FINDINGS ON ADMISSION WITH MAXIMUM, MINIMUM, AND AVERAGE FIGURES; ALSO CLINICAL COURSE AVERAGES PRESENTED IN CONSERVATIVE GROUP

	MAXIMUM	MINIMUM	AVERAGE
Temperature on admission	105° F.	98° F.	101.7° F.
Pulse on admission	160/min.	70/min.	119/min.
Leucocytes on admission	30,000	7,400	19,300
Neutrophiles	99	61	83.7
Duration of fever	27 days	1 day	9.2 days
Duration of first admission	45 days	3 days	18.6 days
Length of interval	40 weeks	1 week	8.8 weeks
Postoperative days	34 days	4 days	9.1 days

general averages. They often present themselves after the infection has become well localized with a large mass in the right lower quadrant, having already accomplished the result sought in the conservative treatment.

Leucocytes.—The leucocyte count was found to be exceedingly variable. The general average of all complicated cases will be seen in Table II. In the late cases and those with generalized peritonitis the figure is often low, indicating a poor response to infection. In two of the fatal cases the total white counts on admission were below 15,000 with neutrophile responses of 89 and 92 per cent. The typical white blood count was over 20,000 with 85 or more neutrophiles per hundred cells.

Physical Findings.—On admission the physical findings were found most significant in making the diagnosis of peritonitis. In Table III it

TABLE III

SUMMARY OF PHYSICAL FINDINGS ON ADMISSION AND RECORD OF APPENDICEAL MASS, CORRELATED WITH AVERAGE LENGTH OF PRESENT ILLNESS

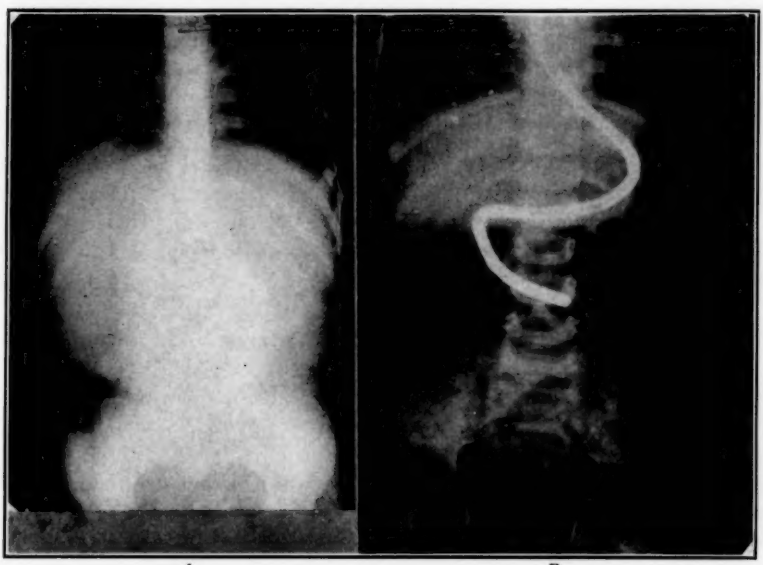
FINDINGS	ON ADMISSION	MASS ON ADMISSION	DEVELOPED MASS AFTER ADMISSION	PER CENT WITH MASS ON ADMISSION	PER CENT WITH MASS AFTER ADMISSION	AVERAGE LENGTH OF PRESENT ILLNESS
Localized to right side	43	29	32	67	74	6.3 days
Generalized	67	17	35	25	52	3.6 days
Total	110	46	67	42	61	

will be noted that 43 cases presented signs confined largely to the right side. Of these 29 or 67 per cent had a large mass in the right lower quadrant. There were 67 cases with generalized findings on admission; that is, with tenderness, spasm, rigidity, and marked rebound tenderness on both right and left sides. Of these 17 or only 25 per cent presented a palpable mass on admission. A striking difference will be noted in average length of illness in these two groups, the latter group, those with generalized findings, being 3.6 days in contrast to 6.3 days in the group with localized signs. Of all cases 67 developed a mass during hospitalization. These masses we believe are made up of matted loops of bowel and omentum and cannot rightfully be considered appendiceal abscesses. In

the entire group but 10 cases developed an appendiceal abscess which required surgical drainage. The mass may form as early as forty-eight hours. In many cases it does not form until late, ten to twelve days. The usual time for the development of a palpable mass is about five days after the onset of symptoms.

The general condition of the patient should always be evaluated as completely as possible. The state of hydration and degree of toxicity may be of considerable assistance in deciding upon operative or conservative therapy.

X-ray.—A "scout film" of the abdomen was found to be of considerable assistance in some cases. As pointed out by Dr. Leo Rigler, the peritoneal line on the right is frequently obliterated (Fig. 4*A*).



A. *B.*

Fig. 4.—*A* and *B*. Scout films of the abdomen to show loss of peritoneal line on the right side and nasal tube in place passing through the stomach into the duodenum, the multiple holes in the tip to be noted.

Inflammation and edema of the bowel and peritoneum serve to obliterate this line on the right, whereas it could usually be made out on the left. Separation of the loops of bowel by fluid could frequently be demonstrated in cases of generalized peritonitis.

Clinical Course

The average duration of fever in all cases treated conservatively was 9.2 days. Many acutely ill patients were observed to reach normal prior to this time, and on the contrary it often required two weeks of conservative management with continuous gastroduodenal siphonage and daily administration of parenteral fluids.

The length of interval has varied from year to year, the average duration being 8.8 weeks. The usual period used at present is six weeks from the time of discharge. The ideal time for deferred appendectomy has not been determined. At present we are employing the sedimentation rate at the time of discharge and again after the six weeks' interval in an attempt to obtain some information as to the most suitable interval period.

During the period of interval care there have been 11 patients, an incidence of 10 per cent, who have had major exacerbations. In each case an additional hospitalization was required, and the conservative treatment used. One patient returned three times, each time with an exacerbation of symptoms occurring at about three weeks. This case was unusual and the only one in which more than one exacerbation was observed. There were 17 patients who complained of abdominal pain and minor symptoms during the interval period; however, none of this group returned until the appointed time. Such an incidence of exacerbations is certainly sufficient evidence that deferred appendectomy is imperative.

The average postoperative hospitalization was found to be 9.1 days. Occasionally the postoperative course was stormy, particularly if difficulty was encountered at operation or a small abscess opened. There were no deaths in the group of 94 deferred appendectomies.

Surgical and Pathologic Findings

There were 94 deferred appendectomies performed. In all cases evidence of previous acute involvement was demonstrated by the presence of many adhesions, a bound down appendix, with the omentum involved in a large percentage of the cases. Frequently the appendix was found in separate parts with only a small stump remaining on the cecum. There were two cases with minimal findings, described in each case as a small adhesion to the tip of the appendix. In 8 cases a persistent mass was encountered. The surgical notes frequently stated that great difficulty was encountered due to matted bowel, adhesions, omentum, or a small abscess. Cultures from the abscess were sterile in most cases. There were two postoperative abscesses and seven wound infections. No fecal fistulae developed following surgery.

There was little correlation in the pathologic reports. Those cases which offered the most difficulty at operation were reported often to have an inactive appendix on microscopic examination. However, 70 per cent of all deferred appendectomies were reported as "acute appendicitis" and 30 per cent were reported as "inactive appendix."

It was difficult to arrive at any correlation between the surgical findings and the length of interval. The findings were related more to the degree of peritonitis or severity of the primary illness. Those having a prolonged initial course frequently presented the greatest difficulty at operation.

Complications

These have been noted previously under "Clinical Course and Surgical Findings." Pharyngitis, tonsillitis, otitis media, mastoiditis, and bronchitis have all been included with upper respiratory infections. The incidence, we believe, is no greater than can ordinarily be expected from cross infections on the pediatric wards.

Upper respiratory infection	10	Exacerbations, minor	17
Diabetes mellitus	2	Wound infection	7
Appendiceal abscess	10	Postoperative pelvic abscess	2
Exacerbations, major	11	Postoperative atelectasis	1

Mortality

In the group of 110 cases of appendiceal peritonitis, all treated conservatively, there have been 5 deaths, a mortality of 4.5 per cent. All

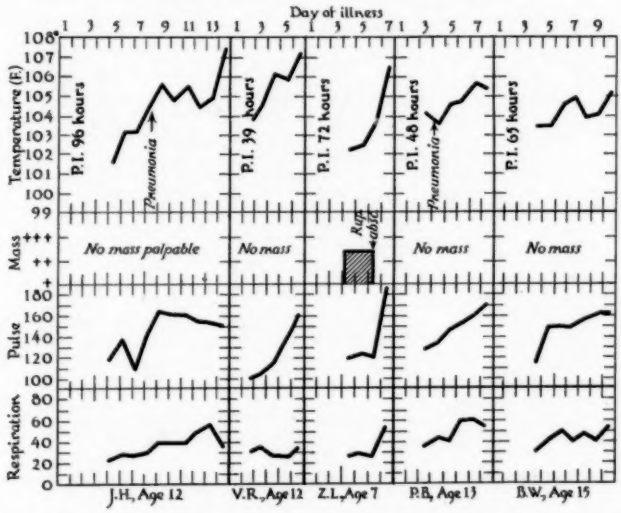


Fig. 5.—A chart showing a diagrammatic record of the five fatal cases with the duration of present illness and complications in each case.

cases of advanced peritonitis have been included unless proved not to be of appendiceal origin. A brief analysis of the records is shown in Fig. 5. It will be noted that the longest history was ninety-six hours and the shortest thirty-nine hours. The temperature, pulse, and respiratory curves are presented to illustrate the rapidly progressive course in each case. It is of additional interest that in no case could a history of purging be obtained. Autopsies were done on three cases; all presented generalized peritonitis and one case showed widespread bronchopneumonia.

Tasche[6] reported the mortality figures for children operated in this hospital from January 1920 to January 1929. The report includes all consecutive appendectomies; 42 were classed as either interval or acute

without evidence of extension. There were no deaths in this group. Sixty-nine cases were classed as having evidence of appendiceal extension. In this group there were 7 deaths, a mortality of 10.14 per cent.

CASES

The following records are presented with a graphic representation of the length of present illness, temperature, pulse, and respiratory curves during the course of conservative management. A diagram of the mass is shown, 3+ indicating a mass filling the right lower quadrant, and 1+ a mass which is small but readily palpable. The high point of each day is presented in the temperature and pulse curves.

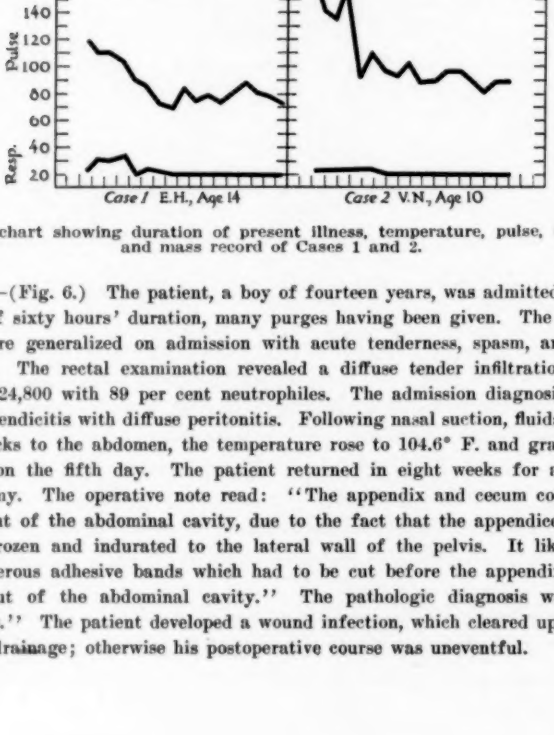


Fig. 6.—A chart showing duration of present illness, temperature, pulse, respiration, and mass record of Cases 1 and 2.

CASE 1.—(Fig. 6.) The patient, a boy of fourteen years, was admitted following a history of sixty hours' duration, many purges having been given. The abdominal findings were generalized on admission with acute tenderness, spasm, and rigidity throughout. The rectal examination revealed a diffuse tender infiltration. Leucocytes were 24,800 with 89 per cent neutrophiles. The admission diagnosis was perforated appendicitis with diffuse peritonitis. Following nasal suction, fluids, sedation, and hot packs to the abdomen, the temperature rose to 104.6° F. and gradually fell to normal on the fifth day. The patient returned in eight weeks for an interval appendectomy. The operative note read: "The appendix and cecum could not be delivered out of the abdominal cavity, due to the fact that the appendiceal tip was markedly frozen and indurated to the lateral wall of the pelvis. It likewise contained numerous adhesive bands which had to be cut before the appendix could be delivered out of the abdominal cavity." The pathologic diagnosis was "acute appendicitis." The patient developed a wound infection, which cleared up following superficial drainage; otherwise his postoperative course was uneventful.

CASE 2.—(Fig. 6.) This case is that of a boy of ten years, admitted following a short history of thirty-six hours, characterized by pain, vomiting, and diarrhea. On admission he appeared dehydrated, his temperature was 104.6° F.; pulse, 164; leucocytes, 28,000 with 94 per cent neutrophiles. The abdominal findings were generalized with tenderness and rigidity, most marked on the right side. Generalized rebound tenderness was present. A diagnosis of perforated appendicitis was made and the usual conservative treatment was administered. The response was favorable although his temperature continued for fourteen days. He was readmitted after six weeks and an appendectomy was performed. At operation many adhesions, including the omentum, were encountered. The pathologic report was "acute appendicitis." The postoperative course was uneventful. This patient illustrates a case of short duration (thirty-six hours) with all of the findings well advanced on admission.

CASE 3.—(Fig. 7.) A boy of four years came in complaining of abdominal pain and vomiting of forty hours' duration. On admission the temperature was 102° F.;

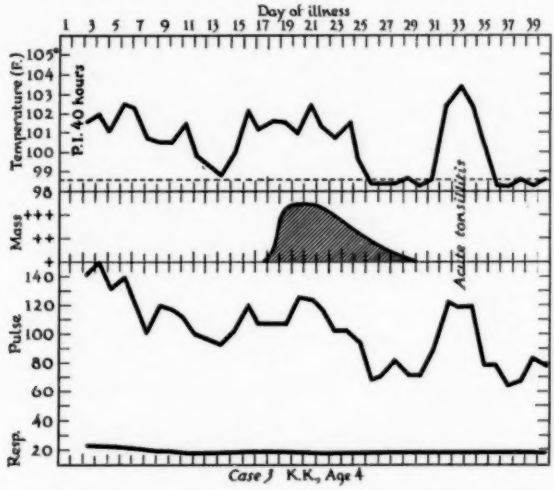


Fig. 7.—A chart showing duration of present illness, temperature, pulse, respiration, and mass record of Case 3.

pulse, 140; and the leucocyte response, 17,500 with 82 per cent neutrophiles. Tenderness was marked throughout but most intense on the right side. Spasm, rigidity, and rebound tenderness were present. No mass could be felt. Conservative treatment was instituted and the temperature reached normal on the tenth hospital day. The temperature and pulse again rose and the patient complained of marked abdominal pain. There was generalized abdominal tenderness and spasm. The patient's diet was restricted to clear fluids only, no suction being used at this time. On the fourth day following the exacerbation a large mass could be palpated, filling the right lower quadrant. The mass after three days gradually disappeared and the patient appeared well. Except for an attack of acute tonsillitis, his course was uneventful. After eight weeks at home he was again admitted for appendectomy. At operation "the appendix was retrocecal and bound down by many adhesions." The pathologic report was "inactive appendix." The course following operation was uneventful. This patient illustrates an exacerbation of symptoms while under care with formation of a large mass which resolved completely.

CASE 4.—(Fig. 8.) A boy of nine years was admitted for the first time following a history of forty-eight hours' duration. The temperature was 101.8° F., pulse, 105; leucocytes, 14,400 with 87 per cent neutrophiles. Examination of the abdomen revealed acute tenderness throughout with generalized rigidity. There was marked tenderness by rectum. He responded quickly to conservative therapy, but on the tenth day had an exacerbation of symptoms with elevated temperature. A mass was felt on the fourth day filling the right lower quadrant. Three days following this, he developed a mucous diarrhea with gross pus in the stool and his mass disappeared. He was sent home in good condition to return three weeks later with another exacerbation of fourteen hours' duration. He again responded to treatment and a mass was felt on the fifth day. This mass gradually resolved and almost disappeared. It was considered advisable to wait before surgery was instituted and he was discharged. After ten days he returned forty-eight hours after a recurrence of symptoms; again a large mass was palpable. This resolved partially and on the fifteenth day an appendectomy was performed. At operation "the appendix was found near the anterior

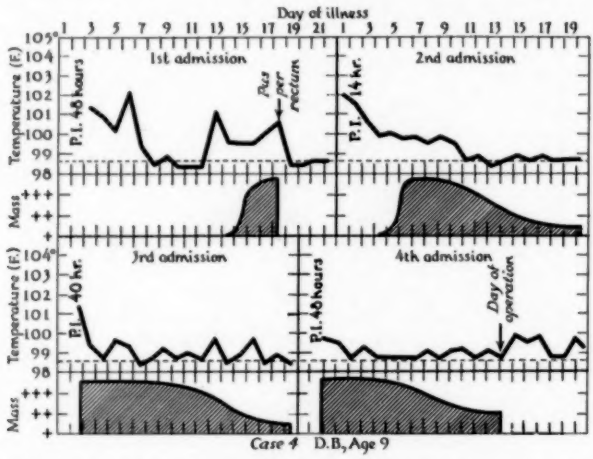

Day of illness
1 3 5 7 9 11 13 15 17 19 21 1 3 5 7 9 11 13 15 17 19
Temperature (F.)
105° 104 103 102 101 100 99 98
1st admission
2nd admission
P.I. 48 hours
Pus per rectum
P.I. 14 hr.
Mass
+++ ++ +
3rd admission
4th admission
P.I. 40 hr.
P.I. 40 hours
Day of operation
Case 4 D.B., Age 9

Fig. 8.—A chart showing the duration of present illness, and records of mass and temperature of Case 4, all hospitalizations.

abdominal wall in the right lower quadrant, matted with omentum and several loops of large and small bowel. These adhesions were rather readily separated and one large adhesive band was cut and tied. Following this it was readily possible to deliver the appendix into the wound." The pathologic report was "acute appendicitis." This case was unusual and illustrates repeated recurrences of localized peritonitis. The occurrence of exacerbations brings up the problem of the best type of interval care, and also the problem of the ideal time following the acute attack for deferred appendectomy. This case, however, is the only one we have observed with more than one exacerbation.

COMMENT

A discussion of the treatment of appendicitis should necessarily specify the stage of the disease. The continuous laudable effort to accomplish early diagnosis and operation must be maintained. When perforation has occurred, the problem becomes a different and a serious one. This

is especially true in the younger age groups where diagnosis is difficult, frequently delayed until complications are present, and the mortality rate appallingly high.

The diagnosis of perforated or complicated appendicitis may be clear-cut; on the contrary, however, the borderline cases remain difficult. We have considered many factors in this decision. Age is important. Eighty-one and six-tenths per cent of our cases of seven years and under were complicated on admission. There was but one death in this group and that in a child of seven years. Previous writers have contended that the conservative method was not indicated in the treatment of appendiceal peritonitis of the aged or the very young child. From our observations on this age group, we must conclude that the conservative management of these difficult cases is a satisfactory method.

The factor of time or duration of symptoms is important in children. We observed the peak of the complicated cases to occur from thirty-six to forty-eight hours. Cases of longer duration were frequently well localized by the time they were first seen, nature having already accomplished the first step in the cure. Duration of symptoms should not be the deciding factor for operative intervention.

The temperature, pulse, and leucocyte responses have been outlined and are all factors of significance in deciding the immediate method of treatment.

The physical findings must be evaluated most rigidly. The presence of a mass was found to be a favorable indication of localization and a definite indication for the conservative regime. With one exception, these patients all did very well.

The incidence of appendiceal abscess requiring surgical drainage was less than 10 per cent in the appendiceal peritonitis group. There were no further complications, such as fecal fistulae.

The x-ray examination of the abdomen was found to be helpful in many cases. It sometimes failed to show the frank changes of peritonitis, such as separation of the loops of bowel or obliteration of the peritoneal line on the right side.

All of the foregoing factors should be considered in determining operative or conservative therapy. The individualization of each case is most essential.

An incidence of 10 per cent in patients treated conservatively who returned with major exacerbations still leaves the problem of length of interval and type of interval care one of the many to be studied further. It appears most evident, however, that deferred appendectomy should be insisted upon in every case.

A discussion of comparative mortality rates is not justified. The reported mortality in children with complicated appendicitis is variable but quite generally high; especially is this true in the younger age groups.

The conservative treatment involves a definite procedure and should not simply be considered as nonoperative interference. The details of the treatment have been outlined previously and should be quite readily adaptable. The interdepartmental cooperation at the University Hospital has been most satisfactory and accounts in large part for the success of the conservative management of appendiceal peritonitis.

SUMMARY

1. In children appendiceal peritonitis presents a real problem as to the most satisfactory method of management. Immediate appendectomy in the uncomplicated group, the conservative treatment and deferred appendectomy in the complicated group have been the methods of therapy employed.

2. A series of 110 cases of appendiceal peritonitis in children have been analyzed.

3. The indications for the use of conservative therapy in children have been presented from the observations. Age, duration of symptoms, temperature, pulse, leucocytes, physical and x-ray findings are all important factors. The individualization of each case is essential.

4. The surgical and pathologic findings have been presented on all deferred appendectomies. All cases showed surgical evidence of previous disease.

5. The clinical course of the disease under conservative management and the complications have been discussed.

6. The mortality in the group of 110 cases of appendiceal peritonitis, treated conservatively, is 4.5 per cent. There were no deaths in the group of 94 deferred appendectomies. In the younger group, seven years and under, the mortality rate was 3 per cent. There were no deaths under seven years.

7. The conservative treatment, which consists of rest, continuous gastroduodenal siphonage, hot applications to the abdomen, paraoral fluids, and sedatives, has been outlined in detail. A presentation of selected cases illustrates variations encountered.

8. An incidence of over 10 per cent in major exacerbations was observed. In every case deferred appendectomy is imperative.

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1009 NICOLLET AVENUE, MINNEAPOLIS

INDIVIDUAL ISOLATION

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A GREAT decrease in the mortality from measles, diphtheria, and scarlet fever, in the wards of the Willard Parker Hospital has taken place in the last fifteen years, apparently starting about the middle of the last decade at a time when individual isolation was instituted throughout the hospital. It has seemed worth while, therefore, to study the subject of individual isolation, its history, its application in a hospital, what it has accomplished and what it can reasonably be expected to accomplish, and particularly the importance of its application to the management of contagion in the home.

The first efforts at individual isolation were evidently those of Grancher about 1889 at the hospital for sick infants (L'hopital des Enfants Malades) in Paris.[6] It seems these efforts were sorely needed. In 1880 Archambault remarked[16] that at this hospital "one does not die of the illness which brought one there but of that which one contracted there." That this was not much of an exaggeration is evidenced by Vallin's figures[19] which showed that from 1885 to 1888, 22 per cent of all the deaths in the hospital, and half of the deaths in the ward for chronic illnesses, were due to infections other than those for which the little patients had been taken to a hospital. In fact, in those days an average of 241 cases a year of diphtheria alone developed in Paris hospitals,[8] and in 1889 Grancher wrote that the mortality of diphtheria in his hospital the preceding few years (1884-1888) had been 64 to 80 per cent.[6] Thus there were annually about 180 deaths from diphtheria due to hospital infection and it is to be presumed considerable numbers of unnecessary deaths from other contagious diseases, particularly measles, of which the hospital mortality rate in those days was 33 to 48 per cent.[6] For twenty years or more there had been isolation hospitals for scarlet fever in England,[15] and isolation wards and pavilions in Paris, but Grancher noted that these did not cut down the occurrence in general wards of contagion due to exposure to unrecognized cases in these wards. Grancher felt that contact infection was of prime importance and air-borne infection of negligible importance, and met considerable opposition to this viewpoint from many of his contemporaries. He was particularly interested in Championnière's report[6] in March, 1888, of the application of the then developing surgical technique, to the

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care of a service of smallpox patients with what were termed "magnificent results." For several years he had been developing details of what he called "medical antisepsis."[6] For instance, he stopped the washing of ward dishes from diphtheria and other patients, in warm water only without further disinfection, and instituted boiling the dishes and disinfecting bed linen and the like, in steam under pressure. Then in 1889 he isolated suspected cases of contagion in the four corners of a general ward with metal mesh screens on the third and fourth sides of the bed (Fig. 1); he required gowns to be put on before one could enter this so-called "box," and he insisted on much scrubbing of hands. He had a nurse care for these isolated patients only, with no contact with the general ward patients. His first year, the incidence of cases of diphtheria on his service due to inside exposure was cut from 15 or 20 a year to one questionable case.[7]

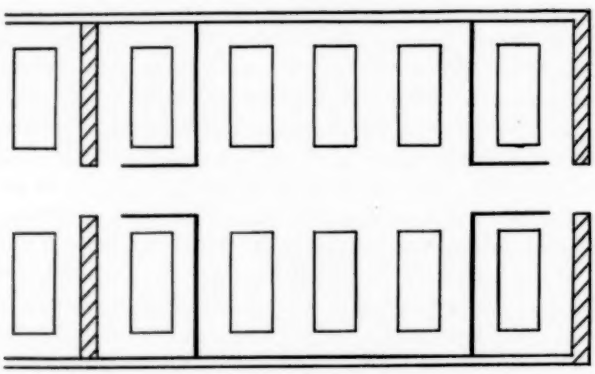

Fig. 1.—Grancher's cubicles.

In the next ten years, 1890 to 1900, in Grancher's wards diphtheria was introduced 43 times, but only once did a case develop in the wards. Scarlet fever was introduced 19 times and 7 cases developed in the wards. Less success was obtained in isolating measles.[2]

Inspired by Grancher, Hutinel in 1894 created at the hospital "des enfants assistes" in Paris, more complete cubicles with glass partitions, and because of results obtained there, the Pasteur Hospital was opened in 1900, the scientific realization of cubicle isolation. The credit of introducing into America the cubicle system of handling contagious diseases is given by Richardson[12] to Charles V. Chapin, and at the Providence City Hospital, now named the Charles V. Chapin Hospital, a building especially constructed for individual isolation was opened on March 1, 1910. Since then the cubicle system has spread not only to other isolation hospitals, but also to many general hospitals where children are cared for.

The cubicle system of individual isolation at the Willard Parker Hospital was installed in the course of many months from 1924 to 1926, the first permanent cubicled wards being occupied in December, 1925. Fortunately for comparative statistics a very exhaustive study of the results obtained on three services at this hospital in a preceding five-year period was made by Haven Emerson and Hopping.[4] At that time there was group or disease isolation, with a few single rooms for unidentified diseases or multiple infections. A visiting physician put on a gown by the front door, made rounds from bed to bed on a service, and not until about to leave did he take off the gown or wash his hands. Now, and for the past decade, there is individual isolation throughout the hospital, with only rare exceptions, such as when two children from the same family come in with chickenpox. By individual isolation is meant the segregation of each patient in a separate unit or infected area, the care of each patient by only those who are especially gowned and free from other contamination, and the concurrent disinfection of any contaminated individual or object before contact is made with another patient.

As was anticipated, a comparison of recent figures, those for the diphtheria, measles, and scarlet fever services, in the past five years with corresponding figures for the five-year period before individual isolation, shows a very striking decrease in the mortality statistics (Table I). There are several viewpoints, however, from which these figures may be analyzed.

TABLE I

CHANGES IN MORTALITY FIGURES AT WILLARD PARKER HOSPITAL

	CASES	DEATHS	PER CENT
Diphtheria			
1919–1923	8776	1427	16.2
1932–1936	2917	119	4.1
Scarlet fever			
1919–1923	3940	323	8.1
1932–1936	7574	87	1.1
Measles			
1919–1923	3720	583	15.7
1932–1936	6614	122	1.8

For example, perhaps the diseases as such were occurring in the city in a milder form, or there were advances in the treatment to lower the mortality generally, outside the hospital as well as inside. And this we see was the case in measles and scarlet fever, in each of which illnesses there was outside the hospital a decrease in mortality rate quite comparable to that inside (Table II). But in diphtheria, while the mortality inside the hospital was cut to one-fourth, that outside nearly doubled. However, these figures for diphtheria cannot be used as evidence of the benefits of individual isolation alone. Too many other

TABLE II

MORTALITY PERCENTAGES INSIDE AND OUTSIDE WILLARD PARKER HOSPITAL

	MEASLES (MANHATTAN ONLY)	SCARLET FEVER	DIPHTHERIA
Manhattan and Bronx without Willard Parker Hospital			
1919–1923	1.78	1.83	2.42
1932–1936	0.13	0.28	4.55
Change	–92.7%	– 84.7%	+ 88.0%
Willard Parker Hospital			
1919–1923	15.67	8.1	16.26
1932–1936	1.84	1.1	4.08
Change	– 88.9%	– 86.4%	– 74.8%

factors are probably more important, such as the inclusion in the statistics of diphtheria carriers with true cases of the disease, and advances in the treatment of toxic cases and of laryngeal cases. For example, aspiration for laryngeal diphtheria which began to be used in 1923 has almost stopped the use of intubation with its attendant very considerable mortality (Table III).

TABLE III

INTUBATIONS IN DIPHTHERIA IN THE WILLARD PARKER HOSPITAL

	1919–1923	1932–1936
Cases of diphtheria	8876	2917
Deaths	1427	119
Cases intubated	1254	54
Deaths	659	17
Per cent of all cases dying after intubation	*7.4%*	*0.58%*

However, the hospital's figures perhaps should not be compared too rigidly with those of elsewhere on Manhattan Island, because for the most part it is the sickest cases who are sent to the hospital, as well as patients from orphan asylums and other institutions, many of whom have been exposed to several contagious diseases. It might therefore be better to compare the hospital's recent figures with those of a decade and a half ago from three viewpoints:

1. Cross infections—that is, what about the child who comes in with one contagious disease and contracts another? Has individual isolation diminished his likelihood of doing that?

2. Secondary infections—that is, such complications as bronchopneumonia and otitis media. Has individual isolation affected them?

3. Length of stay in the hospital. Has individual isolation shortened the need for hospital care?

First, as to cross infections. It must be recognized that with the most exact technique of medical antisepsis in the attempt to accomplish individual isolation, there are certain to be a minimum of cross infec-

tions. Various English observers (Cruickshank, White, Brown, and Allison)[1] have shown that it is possible for infection with hemolytic streptococci to be carried in the air, and it is also quite possible that chickenpox may be air borne. So even with a nearly 100 per cent perfect technique and equipment, cross infections may appear, and furthermore, no hospital's technique is stronger than its weakest follower.

All contagious disease hospitals use disease segregation, and some use individual isolation as well—that is, all patients for instance with scarlet fever are grouped in one building or on one floor, and there put in separate cubicles. There would be very few if any cross infections were it not for the unexpected exposures that result from a patient's being admitted with one disease while incubating another. Thus a child with scarlet fever is admitted into a cubicle in a scarlet fever ward, but within a week breaks out with chickenpox or measles. This infection is considered a "before-admission" or "outside" exposure. Those who despite the isolation contract the chickenpox or measles from this patient, or in fact any children in the hospital who develop a second contagious disease after being in the hospital longer than a reasonable incubation period, are considered "after-admission" or "inside" infection cases. A hospital naturally cannot regulate the number of its "before-admission" exposures, but if the technique is good the average unexpected exposure should not cause more than two infections within the ward, and if it causes only one, the technique is indeed excellent.

However, there are many factors that can affect these figures, such as a shortage of nurses or of supplies, forced overcrowding of wards or a high incidence of chickenpox, the hardest disease to control.

For instance, during the spring of the year 1932 there was great overcrowding of all the wards at Willard Parker, with a resulting relative shortage of nurses, so that individual isolation had to be given up in parts of the hospital and group isolation of whole wards substituted (Tables IV and V). As a result, ward infections with chickenpox, and

TABLE IV

1932 AT WILLARD PARKER

Hospital capacity 424		March average census	494		
		April average census	432		
Maximum (March 17) 519		May average census	417		
	TOTAL PATIENTS	CROSS INFECTIONS			
		BEFORE ADMISSION		AFTER ADMISSION	
Entire hospital	5658	75	1.33%	166	2.93%
Three services*					
Entire year	3732	50	1.34	150	4.02
March, April, May during which		25		130	
Measles		11		45	
Chickenpox		6		78	

*Measles, diphtheria, and scarlet fever services.

TABLE V

RELATION OF OVERCROWDING AND SHORTAGE OF NURSES TO CROSS INFECTIONS

	1932		1933		1934	
HOSPITAL CENSUS						
Total patients	5658 overcrowded in spring		6045 better distribution		3999 light year	
NUMBER OF PATIENT HOURS PER HOUR OF NURSING						
Measles	7.05		7.86		4.34	
Diphtheria	6.41		4.85		4.07	
Scarlet fever	11.37		8.37		8.47	
CROSS INFECTIONS						
EXPOSED	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Before admission	75	1.33	78	1.29	25	0.62
After admission	166	2.93	51	0.84	24	0.60

to a lesser extent with measles, developed to a considerable number. Individual isolation cannot be said to have been used, and the hospital's statistics for 1932 may therefore justifiably be eliminated from those illustrating the effects of individual isolation on the reduction of ward infections. The five years of the Emerson study before individual isolation are therefore compared with the last four years only, without 1932, and show a very satisfactory reduction in ward or cross infections due to inside exposure (Table VI). The figures of three other hospitals for

TABLE VI

CROSS INFECTIONS AT WILLARD PARKER

	TOTAL CASES	CROSS INFECTIONS			
		BEFORE ADMISSION		AFTER ADMISSION	
		NUMBER	PER CENT	NUMBER	PER CENT
*Three Services Only**					
1919—1923 (Disease isolation)	16,436	173	1.05	241	1.40
1933—1936 (Individual isolation)	13,373	196	1.47	153	1.14
All Contagious Services					
1933—1936 (Individual isolation)	22,537	279	1.24	185	0.82

*For 1919-1923, the only figures now available are for the measles, diphtheria, and scarlet fever services.

the same four years are given, but an exact comparison is perhaps not permissible because of differing facilities, and technique. Willard Parker is the only one of the four hospitals with approximately 100 per cent individual isolation, and apparently has the best figures for the prevention of infections after admission (Table VII).

But cross infections are by no means the whole story. Secondary infections, causing such complications as otitis media and bronchopneumonia, must also be considered. Sevestre[14, 16] in 1890 wrote that the seriousness of measles in hospitals resulted almost always from complications brought on by secondary infections. Bronchopneumonia, he added,

TABLE VII

CROSS INFECTIONS IN FOUR ISOLATION HOSPITALS
1933—1936*

	TOTAL PATIENTS	CROSS INFECTIONS			
		BEFORE ADMISSION		AFTER ADMISSION	
Willard Parker	22,537	279†	1.24%	185	0.82%
Kingston Ave., Brooklyn	15,298	105	0.69%	109	0.71%
Essex County,[17] New Jersey	13,015	86	0.66%	169	1.29%
Herman Kiefer,[11] Detroit	14,665	131	0.89%	264	1.80%

*1932 figures are not available for Essex County Hospital, and are therefore left out for all hospitals.

†A disproportionate number of patients come from orphan asylums, with multiple exposures.

is in general neither a manifestation of measles nor the result of chilling, but is positively an indication of secondary infection. This idea of his has been well substantiated since then. The incidence of pneumonia in scarlet fever and diphtheria is not large enough to make comparisons worth while, but in measles it is present in over 90 per cent of the fatal cases. In our figures, less than half as many measles patients per 100 contracted pneumonia in the hospital as before individual isolation (Table VIII). Had the same rate for contracting pneumonia in the hos-

TABLE VIII

PNEUMONIA COMPLICATING MEASLES AT WILLARD PARKER

	TOTAL MEASLES	PNEUMONIA		
		TOTAL CASES	DEVELOPING AFTER ADMISSION	
			NUMBER	PER CENT OF ALL MEASLES
1920—1923	3214	757	245	7.62
1932—1936	6614	593	240	3.63
If				
1932—1936	6614			7.62
Then			504	
or over 4 additional cases of pneumonia each month				

pital held true in recent years as in the period before individual isolation, we would have had an additional 264 cases in five years, or over four more cases each month. Most of these measles pneumonias are due to streptococci, which can be picked up from any infected neighbors, not merely from other pneumonia cases, so that the number of other pneumonia cases to which they were exposed is of little importance. As a matter of fact, it is difficult to decide in many instances whether or not a case of pneumonia started before or after admission to the hospital. At any rate, we have appreciably fewer cases of pneumonia than formerly.

In otitis media the figures for measles are less significant. But in scarlet fever there is apparently a definite betterment in the likelihood of avoiding otitis media, the decrease in our figures being about 25 per cent (Table IX). It is perhaps surprising that there is not a greater difference shown.

TABLE IX

OTITIS MEDIA AT WILLARD PARKER DEVELOPING IN THE HOSPITAL

	TOTAL CASES	ACUTE PURULENT OTITIS MEDIA DEVELOPED AFTER ADMISSION	
		NUMBER	PER CENT
Measles			
1919—1923	3720	527	14.2
1932—1936	6614	821	12.4
Scarlet Fever			
1919—1923	3940	340	8.60
1932—1936	7574	515	6.79
A proportional decrease of 118 and 136 cases respectively.*			

*14.2 per cent of 6,614 cases is 939 cases, 118 more than the 821 which actually developed; likewise 8.6 per cent of 7,574 cases is 651, 136 more than the 515 which actually developed.

In England scarlet fever has recently been demonstrated to be potentially greatly affected by individual isolation. Observers, notably Allison and Brown, have shown that a scarlet fever patient infected with one strain of the hemolytic streptococcus of scarlet fever can pick up another strain, and that the great majority of complications occurring after the second week of hospitalization in multiple bed wards are due to new infection. For example, ten cases of so-called relapses were all due to new infection with a different strain from that which caused the primary attack. While those afflicted in a family epidemic or a "milk route" epidemic may all be infected by a given strain, the patients in a general scarlet fever ward freely "swap" their streptococci. The newly acquired strains are usually the cause of the late infections, and in a comparatively small series of cases Allison and Brown showed that individual isolation definitely decreased this swapping of streptococci and the incidence of secondary infections.

As to the average length of stay in hospital, again many factors can affect the figures—in particular, a change in the regulations for isolation—but they affect measles least of the three diseases. Here there has been a notable change in the figures for those patients who survived (Table X). The money saved by a decrease approximately of from sixteen to ten days in average stay must go far toward paying for the added costs of individual isolation.

If individual isolation can cut down cross infections, secondary infections, and the length of bed care in a hospital, it can do so also in private homes. A chickenpox case with a secondary furunculosis or impetigo should be kept well isolated from other so-called clean cases

TABLE X

LENGTH OF HOSPITAL STAY

	ISOLATION PERIOD	AVERAGE NUMBER OF DAYS		
		ALL PATIENTS	PATIENTS WHO RECOVERED	PATIENTS WHO DIED
Scarlet Fever				
1919—1923	30 days	33.2	34.6	10.5
1932—1936	30 to 21*	26.2	26.4	9.4
Diphtheria				
1919—1923	14+	17.2	18.2	7.3
1932—1936	14+	15.7	15.9	6.3
Measles				
1919—1923	5	15.7	16.4	11.6
1932—1936	6 to 5	9.93	*9.94*	9.4

*The change of isolation period from thirty to twenty-one days was made for adults on March 30, 1932; and for all uncomplicated cases on June 9, 1934.

of chickenpox in his family. While two or more scarlet fever cases in the same household are presumably due to the same strain of the hemolytic streptococcus, one child may be harboring a secondary infection, so every scarlet fever case should be well isolated from every other case. A whooping cough patient with a secondary infection such as otitis media, should of course be well isolated from other whooping cough cases. For measles patients, individual isolation is particularly important, should two or more cases develop simultaneously in a home. In one family, three children who were kept in two adjoining beds, one a double bed, developed a total of five middle ear infections, had three mastoid operations, and one case of bronchopneumonia. The secondary infection here did much more damage than did the original measles.

It is hoped that the statistics shown in this discussion will stimulate the authorities at other hospitals to have the figures compiled of their own ward infections for comparison with those given here. So many factors present in one hospital and not in another can affect the figures that an exact comparison may not be justified, but perhaps in those hospitals where individual isolation is not the rule, its installation may be considered necessary, when the figures of infection are made clear. Particularly, individual isolation in the home is strongly urged, especially of each measles case, and of each case of any contagious disease when there is suspicion of the presence of a secondary infection.

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AN EPIDEMIC OF MOUTH INFECTION OF THE NEWBORN

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IN EVERY maternity service, infections of the newborn are a source of constant concern, and the nursery is, and very correctly should be, most closely guarded against contamination. In spite of the many precautions however, organisms occasionally gain entrance and infections of one kind or another, and of varying degrees of severity, occur. Skin infections are seen entirely too often, thrush occurs occasionally, and less frequently, infectious diarrhea, omphalitis, and conjunctivitis. In the large majority of instances these various infections are single and by prompt isolation and rigid technique show no tendency to spread, so that it is rare that the aspects of an epidemic are seen.

Moreover, as a general rule, the infection is one of the usual type which has been studied and discussed in detail, so that little is added to general medical knowledge by reporting outbreaks unless there are unusual features which make them of especial interest. On the other hand, a new disease, or a new manifestation of a known condition is always interesting and even though positive statements cannot be made, a frank presentation of facts may be of benefit to others.

The following account of an epidemic of sore mouths in newborn babies at the Baltimore City Hospitals appears to fall in the above classification and to warrant reporting.

The maternity division of these hospitals is relatively a new department, having been in operation for about two and one-half years and is housed entirely on one floor of a new building, with adequate and modern equipment. It consists of 96 beds with delivery suite, service units, etc., and is run independently of the remainder of the hospital. Supplies and food are received direct from the central units of the general hospital and do not go through any other divisions. Abortion cases are not received on the division or handled by the house staff.

There are two large nurseries on the floor, each crib being in a separate glass and metal cubicle and adequate isolation nurseries with separate equipment and personnel. There is no nurses' training school at the hospital, all of the nursing care being given by graduate, registered nurses with the assistance of "nurses' aids" for the less technical and more laborious details. The nurseries had been singularly free of infection of any extent or severity until the present outbreak.

On June 2, 1937, it was noticed that two of the babies in the nursery for white infants had reddening of the buccal mucosa and particularly that portion covering the soft palate near its junction with the hard palate, and in one of the mouths there were a few white patches of

exudate. These babies were eight days old, their deliveries had not been unusual nor had they required any great amount of resuscitation. They did not appear ill, had no fever or diarrhea and the condition was thought to be a mild thrush and was so treated, the babies being immediately isolated. From this beginning the infection spread rapidly throughout the white nursery and on June 4, 8 babies showed the typical lesion described later. The following day it appeared in the colored nursery which was staffed by an entirely different personnel and by June 6, four days after the original cases were seen, 31 of a total of 50 babies had contracted the condition in spite of every possible precaution and isolation. In a further attempt to check the spread, another new nursery was set up, with new supplies and equipment from the central supply room and a separate nursing staff. To this nursery only the new babies were admitted, in addition to which new mothers were carefully and strictly segregated from those already in the hospital. On June 8 all but 4 of the babies in the old nurseries were infected, the new nursery remaining free until June 11, six days after it had been in operation, when 1 case developed. At this time it was decided to close the division and this was done, patients being discharged as soon as feasible.

After a thorough cleaning, sterlizing, and airing for ten days, patients were again received, beginning June 28. Two months later no new cases had appeared and apparently the epidemic was ended.

The lesions in all cases were the same, differing only in degree and gaining slightly, but only slightly, in virulence as the epidemic continued. It was difficult to determine with exactness the incubation period. One baby showed evidence of involvement when it was but thirty-six hours old and there was one who had seemingly been exposed for seven days before it was infected. One baby was discharged from the hospital with no evidence of infection at all and thirty hours later was readmitted quite ill with a very extensive involvement. In almost all instances the first symptom noted was an excessive mucus secretion which was somewhat distressing to the child and in some cases required aspiration. Following this the mucous membrane of the soft palate and particularly that portion near its junction with the hard palate was seen to be very reddened, but not swollen and in a few hours was covered with a membrane, the color of which was almost pure white, in contrast to the grayish color of a diphtheritic membrane. This membrane could with difficulty be separated from the underlying mucosa which was then seen to be reddened but did not bleed from the line of cleavage.

In all but a few of the cases this constituted the entire picture, the babies did not appear ill, had no temperature elevations or diarrhea and after a course of about ten days, appeared perfectly well again.

There were 7 exceptions to the above, these babies showing pharyngeal involvement by extension, which caused some cyanosis and interfered with swallowing. These 7 babies became somewhat dehydrated, had a low grade fever and some diarrhea. Two, who appeared most cyanotic, coughed up definite casts of the trachea, 5 to 6 cm. long, and almost immediately showed definite clinical improvement.

The mortality was zero, apparently not so much because of any treatment, as because of the seemingly mild nature of the infection. A few of the infants were for a time classed as being dangerously ill, but all recovered.

It is of interest to note that in spite of the fact that most of the babies went to the breast quite regularly and several of the mothers had cracked nipples, no instance of breast infection occurred.

The pediatrics division of the hospital was asked to cooperate in the emergency and did so with great willingness, assuming almost entire charge of the treatment. The epidemological division of the Baltimore City health department was called upon for help in determining the source and nature of the infection.

Treatment was interesting. When the condition was first seen and thought to be a thrush, the roofs of the mouths were covered with a paste of sodium perborate and water, this being discarded in a few days for first, aqueous, and then alcoholic, gentian violet. The latter was also used as a prophylactic measure, but without avail. Later it was noted that some of the babies who had been discharged and who had received no treatment at all at home were improving more rapidly than those whose mouths were being painted. All active treatment was then discontinued and recovery seemed to be accelerated. There had been an occasional mild diarrhea but after stopping the gentian violet this cleared up rapidly. Those infants who were cyanotic because of extension of the membrane, were given oxygen inhalations until they had improved.

Numerous smears and cultures were taken from the mouths of all babies and from the entire house staff and nursing personnel. Everything that could possibly come in contact with the babies' mouths was most rigidly investigated and every possible effort was made to discover the nature and source of the infection; all to no avail. Mouth cultures and smears showed no Vincent's organisms, nor those of thrush, indeed no one organism was present in all cases. It is true that an alpha-streptococcus was found in 60 per cent of the mouths examined, but since it is also present in just about the same percentage of normal mouths, it is not felt that a great deal of significance should be attached to this finding. The clinical picture was unlike anything encountered by any of the investigators prior to this and a careful and fairly complete search of the literature failed to disclose any report of an outbreak

of like nature. In none of the other hospitals in Baltimore has there been such an outbreak nor even an occasional case. There were several facts which pointed to a mechanical or chemical irritation; the appearance of the mouths with the almost pure white membrane, the absence of systemic symptoms and the fact that in spite of the very rapid spread, there was practically no gain in virulence and that the mothers' breasts did not become infected. These all point against infection, but not the slightest argument in favor of this premise could be found and the final conclusion of all those taking part in the investigation was that the condition was an infection, the source and nature of which remained undetermined.

SUMMARY

An account of an outbreak of sore mouths in newborn babies in a fairly large maternity service is presented.

This outbreak rapidly grew to epidemic size and in six days 46 of a total of 50 babies were infected.

Interesting features of the condition in addition to its rapid spread were: The seemingly mild nature of the infection, its failure to gain, except very slightly, in virulence and its lack of response to treatment.

The lesions were all confined to the mouths of the babies and all were very similar, but quite unlike anything in the experience of any of the observers.

The mortality was zero.

The nature and source of the infection were not discovered. It was found necessary to close the obstetrical division and clean, sterilize, and air everything before the condition was brought under control.

ACCIDENTAL TRANSMISSION OF MALARIA THROUGH THE INJECTION OF WHOLE BLOOD

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BEFORE accepting an individual as a donor of blood or serum for therapeutic use, it is universally recognized that exclusion of syphilis is imperative. Less attention is given to other infections chiefly because most diseases which are capable of being conveyed by transfusion are acute illnesses which can be recognized from physical signs and symptoms. Malaria, however, is a disease common among former inhabitants of tropical and subtropical regions, and capable of existence in a latent form. The infection at this stage may give no subjective symptoms and frequently cannot be detected by clinical methods, yet it is sufficiently virulent to engender an active infection in an individual receiving blood from such a host.

In the literature, I have been able to discover only 24 reports of this type of accident following transfusion or intramuscular injections. Five of these have been made by American authors. This is undoubtedly a poor index of its frequency, since many similar accidents must occur in malarial regions where differentiation between artificial and mosquito transmission is very difficult. Then too, since the incubation period following transfusion may be as long as two months, some cases probably disappear from medical surveillance before the onset of symptoms. In others, the connection between the transfusion and the onset of malaria is not suspected.

At the Babies Hospital during the past year two cases have been observed in which a latent malarial infection was transmitted to the child from one of the parents. A search of the hospital records revealed three additional cases; through the kindness of Dr. E. A. Park, I have been allowed to include one from the Harriet Lane Home of the Johns Hopkins Hospital. Consideration has been given only to instances in which the blood was given for therapeutic reasons, the donor considered suitable, and no suspicion of malarial infection entertained. Consequently, I shall not attempt to review the recent reports of malaria among drug addicts using common hypodermic syringes,[1] nor shall I consider malaria inoculata.

In 1884, four years after Laveran discovered the parasite of malaria, Gerhardt[2] first demonstrated that malaria could be passed directly from man to man without the intervention of the mosquito, by injecting blood

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from a malarial subject into the vein of a healthy individual. Gerhardt, however, did not realize that the mosquito played an essential part in the ordinary transmission of malaria. By 1910, Ross[3] was able to record 51 instances in which an experimental passage of the disease from man to man had been accomplished. Some of these injections were made intravenously and some subcutaneously.

The first accidental transmission of malaria was reported by Woolsey[4] in 1911. Blood transfusion was then a major operation in which the donor's and recipient's vessels had to be joined by surgical anastomosis. The patient was a man of fifty-nine years, suffering from pernicious anemia; the hemoglobin had fallen to 14 per cent and the red blood cell count was only 900,000. The record of his case in the files of the Presbyterian Hospital of New York City recounts the unsuccessful first attempt to effect a transfusion: "Instead of the usual artery-to-vein transfusion, it was attempted to do it from vein-to-vein. Alas! The pressure was higher in the patient's veins than in the donor's." Had someone thought to apply a tourniquet to the donor's arm, the patient would have been spared an infection with malaria, since the donor demurred when requested to submit to a second trial. Eleven days later, another donor was obtained and a successful transfusion performed through an artery-to-vein anastomosis. The recipient's temperature rose rapidly during the following twelve hours, he became first irrational, then comatose, and developed crops of petechiae over his body. The cross-agglutination was rechecked and found satisfactory. On the day following transfusion, tertian malarial parasites were found in the patient's blood smear. The second donor denied ever having had malaria, but after several attempts, the parasites were demonstrated in his blood. Although quinine was effective in curing the patient of malaria, he succumbed shortly afterward to his anemia. The very short period of incubation following transfusion is noteworthy. Nothing is said about the donor used at the first unsuccessful transfusion, so that it is impossible to exclude him as the source of malaria. However, the finding of parasites in the second donor's blood incriminates him. The extreme debility of the patient and the fact that his red blood cell concentration was more than doubled during transfusion (from 628,000 to 1,550,000) may account for the very rapid onset of malarial symptoms.

Gubb[5] in 1919 reported a case in which the infection was passed from the recipient to the donor. The patient was a soldier who was extremely ill with malaria. The exact method of transfusion is not described, but apparently the veins of both parties were exposed with the same set of instruments. After sixteen days, the donor became seriously ill with malaria and "*P. praecox*" (probably falciparum) was found in his blood. After a stormy course, he finally recovered under quinine therapy. This is the only instance I have found in which the estivo-autumnal parasite was so transmitted.

In the following year, 1920, Oehlecker[6] recounted the occurrence of tertian malaria in a patient who had been transfused fourteen days previously from a donor who had never had symptoms of malaria, but who had lived in the tropics two and one-half years before. While in the tropics, he had taken quinine regularly. Parasites could not be found in his blood, but it is interesting to note that he had a chill and pain over his spleen thirty-six hours after giving blood for the transfusion.

Also in 1920, Van Dijk[7] reported the onset of tertian malaria eighteen days after the intravenous injection of 60 c.c. of convalescent serum into a woman who had never been out of Holland. The donor had suffered repeated malarial relapses until seven months before the collection of convalescent serum. No parasites could be demonstrated in her blood, however.

Korabelnikoff[8] in 1927 recorded the case of a man who received two transfusions from the same donor and developed tertian malaria thirty and eleven days after the first and second transfusions, respectively. The donor had suffered an illness similar to malaria one year previously. No parasites were found in his blood smear.

Flaum[9] in 1929 reported the transmission of malaria to four different individuals from the same professional blood donor. The latter had never had symptoms of malaria, and had not been in a malarial district for ten years. Within the space of eight weeks he was used for four transfusions in different Vienna hospitals, and tertian malarial parasites were subsequently demonstrated in his blood and in that of all four recipients. In one instance the incubation period was fourteen days.

A similar occurrence was described in the same year by Schnitzler[10] with nearly identical circumstances. The donor again denied malaria, and when, after the first recipient contracted the disease, his blood was found free of parasites even after he had been given adrenalin, quinine, and splenic massage, he was acquitted as the source of the infection and allowed to give a second transfusion. The second recipient also contracted malaria, and after an exhaustive search, tertian malarial parasites were finally demonstrated in the donor's blood. Further investigation disclosed the fact that he had given two previous transfusions, and that both recipients had also contracted malaria. The incubation period in the first case noted above was nine days.

Netter[11] in this same year cited another instance in which the donor was the victim. The latter was a woman who had never been in a malarial district. She gave blood to a man suffering from an undiagnosed febrile illness which had been present since his return from the tropics eight months previously. Transfusion was accomplished by Jube's syringe, and technical difficulties were encountered which made it likely that some of the recipient's blood refluxed into the donor's veins.

The latter had a chill eleven days after the transfusion and *Plasmodium vivax* was found in her blood smear. Unfortunately, no examination of the recipient's blood was made.

Willetts,[12] also in 1929, reports the first case in which subcutaneous injection was thought to be responsible for the accidental transmission of malaria. The patient was a day-old infant who received blood from his father. The latter was born in Greece but had not had clinical malaria. At the age of four weeks, the infant was seen with full-blown quartan malaria. No parasites could be found on an ordinary smear examination of the father's blood. Here the possibility of transmission through the placenta cannot be excluded, since the mother was also born in Greece. She was not suffering from any malarial symptoms at the time of parturition.

Brief reference is made by Marchoux[13] to a case of Nocht's in which tertian malaria was transmitted from son to mother by transfusion. The woman contracted the disease "after a normal incubation period." The son had not experienced symptoms of the disease during the eight years preceding the transfusion. No studies of the bloods are reported. A similar brief report is made by Majanz[14] in 1930, in which malaria followed three weeks after transfusion. The type of malaria is not stated and no examination of the donor's blood was made. The latter denied ever having experienced the disease, but had inhabited a tropical region.

A third instance of infection of the donor by the recipient during a direct transfusion is described by Décourt[15] in 1931. The recipient of the transfusion had malaria nine years previously, was cured with quinine, and had remained free from symptoms until the incision of a subcutaneous abscess, a few days before the transfusion, led to the onset of bouts of chills and fever, and a progressive anemia. Beginning one week after the donation of blood, the donor had recurring febrile attacks every other day. Malarial parasites were found in the bloods of both parties, and they responded rapidly to quinine therapy.

Jankelson[16] in the same year mentions the transmission of malaria to a six-weeks-old infant by intramuscular injection from an individual who had had malaria thirty-seven years before in Italy. Asexual forms of *Plasmodium malariae* were found in his blood. No statement is made of the incubation time.

The only comprehensive review of this subject in the American literature was contributed by Stein[17] in 1932. He cites nine of the above cases, and two more which I have not included. One of these latter is reported in a journal which is inaccessible to me,[18] and the other records the transmission of malaria through an improperly sterilized hypodermic syringe, but under conditions in which it is impossible to exclude transmission by mosquitoes.[19]. Stein adds a case of his own in which quartan malaria was discovered in a Greek girl of two and one-half years, nineteen days after she had received a transfusion from her father. The

source of her infection was not suspected, and after a cure with quinine, a second transfusion was given from the same donor. Again, malaria appeared in the patient after an interval of twenty-five days. The child's father, who donated the blood, had experienced malaria eight years before, and after an extensive search quartan parasites were finally found in his blood smear.

Nobécourt and associates[20] observed the passage of quartan malaria from a common blood donor to two different recipients. The incubation time was not determined in the first case, and was twenty days in the second. The donor had been in the African colonies eight years previously, and although he had never had symptoms, his spleen was enlarged. Parasites could not be found in his blood, but his serum gave a positive Henry reaction (a pigment flocculation reaction, supposedly diagnostic of malaria).

A unique method of proving the origin of the parasites was used by Usandizaga and Marco.[21] Their patient contracted malaria thirty-four days after receiving a transfusion from her son. The latter had had malaria a year before, but parasites could not be found in his blood. Five cubic centimeters of his blood were injected intravenously into a schizophrenic patient, who six weeks later contracted tertian malaria, also. Osorio and Costa[22] observed the appearance of quartan malaria ten days after an intramuscular injection of blood in a three and one-half month old infant, born in a region of Chile where quartan malaria was unknown. The child's father, from whom she received the blood, was a Syrian who had suffered annual attacks of chills and fever since leaving his native country. Smears of his blood were free from parasites even after the injection of adrenalin and milk. The patient recovered promptly following the institution of quinine and plasmochin therapy.

Naveiro[23] had a patient who presented symptoms and laboratory confirmation of quartan malaria twenty-eight days following transfusion from a donor who had been asymptomatic for thirty-seven years. Parasites were not found in the latter's blood, and his spleen was not palpable.

Harvier, de Brun, and Lafitte[24] noted a very short incubation period of three days following transfusion. Their donor had returned from a seven-year sojourn in the tropics, four and one-half months before. He had never had symptoms of malaria, and presented no clinical evidence of the disease, but *Plasmodium malariae* were found in his blood smear. The patient is said to have had *Plasmodium vivax* on blood smear, and no interpretation of this discrepancy is offered. Perhaps the term "*Plasmodium malariae*" is used in an inexact sense.

Epstein's case,[25] like that of Willetts above, may be an instance of the placental passage of plasmodia. The recipient was an infant of three days who received intramuscular blood from the mother, and developed

quartan malaria seven weeks later. The mother had lived in Palestine, had an enlarged spleen, but her blood did not contain demonstrable parasites.

Pinard[26] makes the statement that malaria developed three and one-half weeks after transfusion in one of his patients despite the fact that one part per thousand of mercurous cyanide was added to the blood. He gives no other details.

Cadham[27] and Thomas, Keys, and Dyke[28] added two more cases in 1936. Cadham's patient was a girl of thirteen years who received a transfusion from her father as an emergency measure following operation; she developed quartan malaria three weeks later. The episode took place in western Canada where malaria is almost unknown. The father, although always asymptomatic, had travelled in regions where malaria was endemic, and quartan parasites were demonstrated in his blood. The patient recovered promptly on quinine therapy.

Thomas, Keys, and Dyke report the case of a man transfused in England where he had spent his entire life. Three days after receiving the second of two transfusions given sixteen days apart, he had a sudden chill and temperature rise. *Plasmodium vivax* was found in his blood. The donor had travelled extensively in India and, although he had not suffered full-blown malaria, he had experienced a few slight chills about fifteen months before donating blood. No parasites were found in his blood.

Wang and Lee[29] report the experience of the Peiping Union Medical College for the years 1925-1935. During this period there were 54 instances in which patients contracted malaria shortly following transfusion. Since tertian malaria is found in that portion of China, the authors admit that it is not possible to exclude naturally acquired infections, or relapses of preexisting latent infections. In the 13 cases which followed the administration of a single transfusion, the incubation periods ranged from three to sixty days, all but four of them falling between the tenth and twentieth days. Data were available on only seven donors. One gave a history of malaria twenty years before; the rest denied the disease. All of these donors had given blood to more than one individual, and one man had supplied blood to twenty different persons, of whom five contracted malaria. Ordinary thin-smear examinations were made on 18 donors with a single positive result. None of them had palpable spleens. The authors noted that patients who received blood on more than one occasion from infected donors never developed malaria more than once. This they attributed to the low virulence of the latent infection and the development of some immunity on the patient's part. Of the 54 patients who were supposedly infected by this method, 14 died; in seven of these, death was thought to have been hastened by the presence of malaria. In 9 others, convalescence was pro-

TABLE I

SUMMARY OF CASES OF ACCIDENTAL TRANSMISSION OF MALARIA

NO.	AUTHOR	YEAR	TYPE	ROUTE	INCUBATION	AGE	RESULT	DONOR'S BLOOD	DONOR'S HISTORY
1	Woolsey	1911	T*	Vascular anastomosis	24 hr.	59 yr.	Cured of malaria	*P. vivax*	No symptoms of malaria.
2	Gubb	1919	A-E	Direct transfusion, R to D†	16 days	Adult	Cured	*P. praecox*	Recipient of transfusion acutely ill with malaria at the time of transfusion.
3	Oehlecker	1920	T	Direct transfusion	14 days	Adult	Cured	No parasites	Asymptomatic. Lived in tropics 2½ yr. before transfusion.
4	Van Dijk	1920	T	Intravenous serum	18 days	35 yr.	Cured	No parasites	Repeated attacks of malaria until 7 mo. before transfusion.
5	Korabelnikoff	1927	T	Transfusions—2	11 or 30 days	Adult	Cured	No parasites	Illness similar to malaria one yr. before.
6	Flaum	1929	T	Transfusion	14 days	Adult	Cured	*P. vivax*	Asymptomatic. Lived in malarial region 10 yr. before. 3 other cases.
7	Schnitzler	1929	T	Transfusion	9 days	Adult	Cured	*P. vivax*	Asymptomatic. 3 other cases.
8	Netter	1929	T	Direct transfusion, R to D	11 days	30 yr.	Cured	No examination	Recipient ill with undiagnosed fever since return from tropics 8 mo. before.
9	Willetts	1929	Q	Subcutaneous blood	< 4 wk.	1 day	Cured	No parasites	Asymptomatic. Born in Greece.
10	Marchoux	1929	T	Transfusion	?	Adult	?	No examination	Asymptomatic. Malaria 8 yr. before.
11	Majanz	1930	?	Transfusion	3 wk.	?	Cured	No examination	Asymptomatic but had lived in malarial region.
12	Décourt	1931	T?	Direct transfusion, R to D	7 days	Adult	Cured	*P. vivax?*	Recipient had malaria 9 yr. before but was asymptomatic in the interim.
13	Jankelson	1931	Q	Intramuscular blood	?	6 wk.	?	*P. malariae*	Malaria 37 yr. previously; asymptomatic since.

*T, tertian; Q, quartan; A-E, estivo-autumnal.
†R, recipient; D, donor.

TABLE I—CONT'D

NO.	AUTHOR	YEAR	TYPE	ROUTE	INCUBATION	AGE	RESULT	DONOR'S BLOOD	DONOR'S HISTORY
14	Stein	1932	Q	Transfusions—2	19; 25 days	2½ yr.	Cured twice	*P. malariae?*	Malaria 8 yr. before; asymptomatic since.
15	Nobécourt	1932	Q	Transfusions—2 recipients	20 and < 19 days	11 and 13 yr.	Cured	No parasites Henry reaction positive	Asymptomatic but in malarial district 8 yr. before. Infected 2 recipients.
16	Usandizaga and Marco	1932	T	Transfusion	34 days	44 yr.	Cured	No parasites	Asymptomatic but in Africa 1 yr. before. Infected a second recipient.
17	Osorio and Costa	1932	Q	Intramuscular blood	10 days	3½ mo.	Cured	No parasites	Recurrent mild malarial attacks for 22 yr.
18	Naveiro	1934	Q	Transfusion	28 days	42 yr.	Cured	No parasites	Asymptomatic for 37 yr. following malaria.
19	Harvier and Coworkers	1934	T	Transfusion	3 days	Adult	Cured	*P. vivax??*	Asymptomatic, but in tropics 4 mo. before.
20	Epstein	1934	Q	Intramuscular blood	7 wk.	3 days	Cured	No parasites	Asymptomatic; enlarged spleen; lived in Palestine.
21	Pinard	1934	?	Transfusion	3½ wk.	?	?	No examination	Not stated.
22	Cadham	1936	Q	Transfusion	3 wk.	13 yr.	Cured	*P. malariae*	Asymptomatic but had traveled widely in malarial regions.
23	Thomas and Coworkers	1936	T	Transfusion	19 days ?	26 yr.	Cured	No parasites	Traveled in India. A few chills 15 mo. before.
24	Wright	1937	Q	Transfusion	4 wk.	19 mo.	Relapse	*P. malariae*	Asymptomatic but born in Italy.
25	Wright	1937	T	Intramuscular blood	2 mo.	1 day	Cured	No parasites	Born in Greece, but no definite history of malaria.
26	Wright	1937	Q	Transfusion	4 wk.	1 yr.	Cured	No parasites	Malaria 33 yr. before; asymptomatic since; failed to infect second recipient.
27	Wright	1937	Q	Intramuscular blood	2½ wk.	3 yr.	Cured	No parasites	Malaria 10 yr. before; asymptomatic since.
28	Wright	1937	Q	Transfusion	< 8 wk.	8 yr.	Cured	No examination	Born in Greece. No inquiry.
29	Wright	1937	Q	Transfusion	6 wk.	9 mo.	Cured	No parasites	Occasional mild symptom following malaria 12 yr. before.

longed. The vast majority of the patients were readily cured with quinine. Since there is some uncertainty about the method of infection in these cases, I have not included them in the tables which follow, but it will be seen that the experience of these authors parallels closely the tabulated cases.

The records of the six cases which I wish to add are presented here. Tables I and II summarize the data of these and the cases mentioned above.*

TABLE II

SUMMARY OF TABLE I

1. Route of transmission:		
Donor to recipient	26	
Recipient to donor	3	
2. Type of malaria:		
Tertian	13	
Quartan	13	
Estivo-autumnal	1	
Not stated	2	
3. Method of injection:		
Intravenous	23	
Intramuscular	5	
Subcutaneous	1	
4. Incubation time:		
Less than 1 day	1	
1-7 days	2	
8-14 days	6	(5?)
15-21 days	9	
22-28 days	6	
29-56 days	5	(6?)
Not stated	2	
5. Result of treatment:		
Cured	25	
Relapse with ultimate cure	1	
Not stated	3	
6. Parasites in donor's blood:		
Present	10	
Absent	14	
No examination made	5	
7. Malarial symptoms in donor before blood donation:		
Previous malaria	13	
No previous malaria	14	
No statement	2	

CASE REPORTS

CASE 1.—V. LaM., an Italian female of 19 months, was first admitted to the Babies Hospital on July 7, 1932. Both parents were born in Italy; the child was born in New York City. The father denied malaria. The birth, feeding, developmental, and previous medical histories of the patient were not remarkable. The illness which brought her to the hospital began four weeks previously with a temperature of 102° F. and a discharging right ear. Her family physician diagnosed pneu-

*Since this article was submitted for publication, another report has been discovered in the literature. McCulloch (Canad. M. A. J. 37: 26, 1937) describes the case of a young woman who contracted quartan malaria in Toronto twenty-six days after receiving a transfusion from her father. The donor had lived in Roumania twenty-five years before and had always been symptom-free, and parasites were not found in his blood. The patient was readily cured with quinine and atabrine.

monia of the right lower lobe a few days later. After a week the signs and the fever disappeared. On the night before her admission to the hospital, the temperature rose suddenly to 104° F. and grunting respirations were noted.

On admission, the physical examination showed an acutely ill infant with a temperature of 103.6° F., rapid, grunting respirations, orthopnea, pallor, and profuse sweating. Both tympanic membranes were dull, the right one discharging thin pus through a perforation. Over the right middle and lower pulmonary lobes there was dullness and distant bronchial breathing, but no râles. The abdomen was distended, and the spleen could not be felt. Examination of the blood revealed 8.2 grams of hemoglobin per 100 c.c., 3,280,000 erythrocytes, and 38,200 leucocytes with 73 per cent polymorphonuclears and 27 per cent lymphocytes. No malarial parasites were seen in the smear. The urine gave a two plus test for albumin; otherwise it was normal. Roentgen examination of the chest revealed a shadow of uniform density obscuring the lateral two-thirds of the right lung field and producing a slight displacement of the heart to the left. Roentgenograms of the mastoids showed diffuse clouding of the cells with some destruction of the septa on the right.

During the first two weeks in the hospital the patient showed slow clinical improvement with gradual defervescence and fall in the leucocyte count to 10,000. Repeated roentgen examination of the chest pointed to an encapsulated empyema on the right side. However, only a few cubic centimeters of pus could be obtained on thoracentesis. The culture showed pneumococcus Type VI. Stereoscopic roentgenograms of the right mastoid were interpreted as visualizing an area of bone destruction along the sigmoid sinus. On July 21 her temperature suddenly peaked to 105° F. and pneumococcus Type VI was recovered from the blood stream. Thrombophlebitis of the right sigmoid sinus was suspected and a simple mastoidectomy performed. The cellular septums were found destroyed, but only a small amount of pus was encountered. The sinus plate appeared normal, so no exposure of the sinus was made. Culture of the wound yielded hemolytic staphylococcus aureus.

Following operation, a low grade fever persisted, the wound healed slowly, and there was little alteration in the findings in the chest. Clubbing of the fingers became apparent and a second chest aspiration produced a small amount of pus containing pneumococci.

On August 15, in preparation for a thoracotomy, she was given a direct transfusion of 100 c.c. of blood from her father by the multiple syringe method. There was no immediate reaction. Following this procedure she improved and thoracotomy was delayed until August 30, when a section of the right sixth rib was removed. A heavy plastic pleural exudate was encountered and drained. Immediate improvement followed, and she maintained a normal temperature for the next twelve days.

On September 12, exactly four weeks after transfusion, her temperature peaked to 103° F. Similar peaks occurred every third day for the next two weeks, with a normal temperature between. No explanation for this phenomenon was apparent, until finally the shape of the temperature curve aroused the suspicion of malaria, and quartan malarial parasites were discovered in the blood smear on September 29. Quinine sulfate was administered in doses of two grains twice a day for a week. An abortive peak of temperature occurred on October 2; subsequently she remained afebrile. Parasites were found in decreasing numbers until October 8, when they disappeared completely. The leucocyte count, which was 10,700 at the onset of her recurrent bouts of fever, had fallen to 4,850 by the time quinine therapy was started. Examination of her father's blood failed to show parasites. She was discharged from the hospital on Oct. 15, 1932, with her surgical wound healed; the parents were instructed to administer three grains of quinine daily.

Her progress at home was satisfactory, and on November 14 she was seen in the out-patient department where no abnormal physical findings were encountered, and a blood smear showed no malarial parasites. Quinine therapy was therefore discontinued. However, three days later she had a convulsion followed by vomiting, temperature of 103° F., and pain in the right chest. Her temperature remained elevated, and she began to cough. She was readmitted to the hospital on November 20. At this time she was acutely ill, with temperature of 102.6° F., an injected pharynx, several petechial spots over the neck and trunk, and a very large spleen extending to the umbilicus. There was slight enlargement of the liver. Her leucocyte count was 4,300 and malarial parasites were again present in the smear. A blood culture was sterile.

On the third day after readmission, another sharp rise in temperature occurred and euquinine was administered. She received 16 grains of this drug on November 24, 8 grains a day for the next five days, and then the dose was slowly reduced until she was receiving 3 grains a day. After one brief rise of temperature on November 26, she remained afebrile and the parasites disappeared from her blood by December 1. A second examination of the father's blood showed quartan malarial parasites. The patient was discharged on December 5 and was followed in the out-patient department for the next year. During this time her spleen slowly receded, she remained afebrile, and a blood smear taken after five months showed no parasites.

In brief, this American-born child of Italian parentage contracted quartan malaria four weeks after receiving a transfusion from her father. She was rapidly cured with quinine, suffered a relapse when the drug was discontinued, and was again cured when therapy was reinstituted. Parasites were seen in the father's blood although he denied that he had ever had malaria.

CASE 2.—N. K., was born in the Sloane Hospital for Women on April 16, 1933. Both parents were born in Greece. The mother could not remember having had malaria, but thought it likely that she had suffered from the disease as a child, since everyone else in the neighborhood had it. The patient was born at term after a midforceps delivery. He was not asphyxiated at birth, but there was a forceps mark over the right mastoid, zygoma, and eye with subcutaneous hemorrhage and a small area of abrasion of the skin. There was a right facial palsy and tremor of the extremities. No other abnormalities were noted. Neither the liver nor spleen was palpable. His weight was 3,650 gm. and length 50 cm.

Soon after birth, 20 c.c. of blood were taken from the mother and injected into the infant's buttocks. On a formula of whole cow's milk, water, and cane sugar, he gained weight rapidly. The facial palsy gradually disappeared. During the third week of life, the hematoma over the right side of face became infected and discharged a little pus, but was healing well at the time of his discharge on the twenty-fifth day of life. He visited the clinic at six weeks, and at this time was afebrile, gaining weight well, and showed nothing unusual on physical examination.

On June 12, at the age of two months, he was admitted to the Babies Hospital because of an irregular fever which had begun six days previously. There was no other complaint from the mother except that his hands and feet became blue and cold with the onset of fever. At the time of admission, his temperature was 102.6° F. There was a fine maculopapular rash over the trunk. His liver and spleen were both enlarged, firm, and extended three fingerbreadths below the costal margin. A small scar was present over the site of the hematoma on the right zygoma. Examination of the blood showed 10.5 gm. of hemoglobin per 100 c.c., 3,530,000 erythrocytes, and 6,250 leucocytes with 33 per cent polymorphonuclears and 67 per cent lymphocytes. The smear showed tertian malarial parasites and a moderate degree of achromia, anisocytosis, and polychromasia of the red blood cells.

No treatment was given for five days, during which time his temperature rose on every second day. There was a gradual decrease in the hemoglobin concentration and erythrocyte count. Parasites were seen on a second examination. On June 17, quinine sulfate was administered in doses of 0.25 gm. daily, resulting in an immediate flattening of the temperature curve and disappearance of parasites from the smear.

On July 3 he was discharged with a hemoglobin concentration of 15.8 gm. per 100 c.c., and an erythrocyte count of 3,860,000. The spleen, although still palpable, was distinctly smaller in size. His quinine dosage was halved and continued at home for another month. When seen six months later, he was asymptomatic and his spleen was no longer palpable.

During hospitalization two blood smears from the mother were examined but no parasites could be demonstrated. Since the infant was not taken out of New York City during his life, and since the mother presented no symptoms at parturition of an active malarial infection, it seems probable that he was infected from the blood injected intramuscularly at the time of birth. Placental passage of the parasites, though possible, seems less likely.

CASE 3.—H. N. was first brought to the Babies Hospital at the age of one year because of vomiting and abdominal distention. Although her parents were American, her father was born in Greece where he lived during his youth. The maternal grandfather died of pulmonary disease, but had not been in contact with the patient. Repeated attempts to have the parents and another child examined for tuberculosis have failed.

H. N.'s birth was normal, her development average and, except for the omission of added vitamin D, her diet was adequate. At six months she had an illness diagnosed as bronchopneumonia, characterized by fever and cough and lasting three weeks. At eight months she had bronchitis for a period of two weeks. Neither of these illnesses was regarded as serious, and she appeared to thrive until the onset of the present complaint seven weeks before admission. She then began to lose her appetite, became fretful at night, and the stools were noted to be larger than usual and filled with mucus. Abdominal distention of increasing severity appeared, and was only partially relieved by enemas. She lost a large amount of weight. On the day before admission, she began to vomit and enemas produced only a small fecal return.

When admitted to the hospital on Feb. 14, 1936, she was an emaciated infant with a very large abdomen. She appeared seriously ill, weighed 7,800 gm. and had a temperature of 102.8° F. She was drowsy and toxic, with deep respirations, sunken eyes, and dehydration of the skin and mucous membranes. Except for harsh breath sounds and a high diaphragm, the lungs were clear. The abdomen was large, doughy, tympanitic to percussion in the midline, but dull in the left flank and just above the symphysis pubis. There was no fluid wave, shifting dullness, or tenderness on palpation. No distinct mass could be identified on abdominal palpation, but on rectal examination a firm, oval mass about 2 by 3 cm. was encountered lying above the brim of the pelvis on the left side. The liver extended 2 cm. below the costal margin; the spleen was not felt.

Examination of the blood showed a pronounced anemia with a hemoglobin concentration of 8.0 gm. per 100 c.c. and an erythrocyte count of 3,180,000. The leucocytes were 13,400 with 57 per cent polymorphonuclears, 40 per cent lymphocytes, and 3 per cent monocytes. No malarial parasites were seen in the smear. The erythrocyte sedimentation rate was 93 mm. in one hour by a modification of the Westergren technique. The carbon dioxide-combining power of the blood serum was 74 volumes per cent. An intradermal injection of 0.01 mg. of tuberculin gave a definitely positive reaction. Blood culture and Kahn test were both negative.

Roentgenograms of the chest and abdomen showed patchy infiltration of the right middle pulmonary lobe suggestive of tuberculosis or bronchopneumonia, and a diffuse clouding of the abdominal cavity with comparatively little gas present. No abdominal mass was visualized.

These findings were thought to indicate tuberculosis involving the abdominal lymph nodes and peritoneum with the formation of numerous adhesions and the production of a partial intestinal obstruction. Surgical measures seemed to offer little hope of relief, and for the next three days fluids were administered entirely by parenteral routes. On February 16 she was given a transfusion of 125 c.c. of citrated whole blood from her father. The only reaction noted was the appearance of a few urticarial spots on the forehead immediately following the procedure.

Despite the fact that her temperature reached a lower level and her hemoglobin concentration and red blood cell count rose, her course during the next three weeks was very stormy. Vomiting and abdominal distention persisted, and because of her poor food intake, nutritional edema associated with a low serum albumin appeared. By the end of the fourth week, gradual improvement had set in and she was taking a high caloric diet well and spontaneously passing normal stools. The abdominal distention persisted, however, and a mass now appeared in the right lower abdominal quadrant. Examination of stools and gastric contents for acid-fast organisms was consistently negative.

On March 15, twenty-nine days after the transfusion, several merozoites of quartan malarial parasites were seen on examination of a routine blood smear. For the preceding week she had run an irregular, low grade fever. On March 18 there was a sudden spike to 103.8° F. and her spleen was palpable for the first time. Quinine hydrochloride was given in doses of 0.48 gm. per day for the next week. On March 20 her temperature began to spike daily to 104° or 105° F. and the number of parasites seen in blood smears increased. No chills were observed. Since treatment was obviously inadequate, the quinine dosage was doubled on March 25. There was a prompt drop in temperature so that from March 28 on it remained normal. Malarial parasites disappeared more slowly from the smear, but after April 4 no more were found. The dosage of quinine was gradually reduced and the drug stopped completely on April 5.

The father stated that he had suffered from malaria for eighteen months in 1902-1903, but had not had symptoms in the ensuing thirty-three years. Several smears of his blood were examined, but no malarial parasites were discovered. Subsequently, an attempt was made to pass malaria from him to an infant who was slowly dying of postmeningitic hydrocephalus. A transfusion of 20 c.c. of blood was effected and smears taken from the infant twice a week for the remaining six weeks of its life. Parasites were never seen on these smears, the temperature curve remained flat, and no gross or microscopic evidence of malaria could be found at autopsy.

Following this episode of malaria, H. N. showed enough improvement to warrant her discharge from the hospital in order to spend the summer at the seashore. There she contracted measles and went into a slow decline with increasing vomiting, abdominal distention, and loss of weight and appetite. At the time of readmission to the hospital on July 16 at the age of seventeen months, she was much more emaciated, the abdomen was greatly distended, and the umbilicus was red and pouting with a small white area in the center through which rupture seemed imminent. There was dullness over the lower abdomen, evidence of free fluid, and masses of matted lymph nodes could be palpated by rectal examination. The umbilicus was incised and pus obtained from which *B. coli* was cultivated. After a week, fecal drainage appeared in the wound and a fecal fistula persisted thenceforth. Acid-fast organisms were demonstrated in the discharge from this fistula. At a later date the opening closed and had to be reopened surgically. An exploratory celiotomy

was attempted but adhesions were so numerous that it was impossible to enter the peritoneal cavity. Despite every effort to cater to her whims of appetite and despite liberal administration of vitamin preparations, cachexia became so severe that in December, 1936, her weight had fallen to 5,620 gm. Although her temperature spiked almost daily to 104° F., repeated attempts to find malarial parasites in her blood were fruitless.

In January, 1937, the left eardrum ruptured and a month later there was spontaneous drainage from the right drum also. A few days later a right facial palsy suddenly appeared and a right simple mastoidectomy was performed. The mastoid and canal wall were found completely necrotic at operation, with a pathologic exposure of the dura mater. A large amount of caseous material and necrotic bone was removed and acid-fast bacilli found in the curettings. The patient progressed slowly to a fatal outcome on April 17, 1937. Autopsy permission was granted and extensive tuberculosis of the lungs, liver, spleen, kidneys, mastoids, meninges, and intestines was found. There was an adhesive peritonitis with two fecal fistulas and two large peritoneal abscesses. No gross or microscopic evidence of malaria was discovered.

In summary, this patient was an American-born infant of one year who contracted quartan malaria four weeks after a transfusion from her father. She was cured of malaria by quinine therapy, but succumbed a year later to extensive tuberculosis and showed no evidence of malaria at necropsy. Her father had been free of malaria for thirty-three years, parasites could not be found in his blood, and transfusion of a second infant with a smaller quantity of his blood failed to induce a similar malarial infection.

Case 4.—F. V., a Puerto Rican boy of three years, was admitted to the Babies Hospital on July 17, 1936, with the diagnosis of malaria. Both of his parents were born in Puerto Rico, but the child had spent his entire life in New York City. The mother had no recollection of having had malaria. The father had suffered from the disease twenty-two years previously while living in Ecuador, receiving no treatment at the time. In 1926, while working on a boat off the coast of Colombia, he had had a severe attack of chills and fever, recurring every third day. The symptoms disappeared after he took quinine for a week, and he had not had any recurrence of symptoms during the intervening ten years.

Except for mumps and varicella, F. V. had been well until May 17, 1936, when he was admitted to Willard Parker Hospital with measles. On the day of admission, he was given an extramuscular injection of 30 c.c. of whole blood from his father. No immediate reaction ensued, and he recovered promptly from measles with no complications. He was discharged from the hospital on May 21.

At home he did not seem entirely well. His appetite was poor and he was pale and irritable. The gradual development of a lemon yellow tinge of his skin and sclerae was also noted. About two and one-half weeks after the onset of measles, recurring chills, fever, and vomiting appeared every third day at 7 P.M. On one occasion he passed red urine. During the six weeks in which these symptoms were present, he lost one or two pounds in weight.

Upon admission, his temperature, pulse, and respirations were all normal, and he did not seem ill. There was a slight yellow color of the skin and sclerae, and mild pallor of the mucous membranes. A few small urticarial spots were present on the face and neck. The spleen was firm and extended 2 cm. below the costal margin. Because of our recent experience with Case 3, malaria was suspected at once. The blood examination revealed 10.7 gm. of hemoglobin per 100 c.c., 2,920,000 erythrocytes, and 4,450 leucocytes. The smear contained many plasmodia of the quartan type, and showed anisocytosis, achromia, and basophilic stippling of the red blood cells.

Treatment was withheld for a few days, and on July 19 he had a chill and temperature rise to 105.2° F. Parasites were again seen in the smear. On July 21 a course of quinine was started. He received 0.3 gm. of quinine bisulfate three times a day for eight days. On July 22 he had his final chill, accompanied by temperature of 102.4° F. On July 27 no more parasites could be found in the blood smear and the spleen had begun to shrink. When he had passed two weeks with a normal temperature and several blood smears had been negative, he was given 0.3 c.c. of adrenalin and more smears taken. Parasites were not discovered, but on the following day he had a chill and his temperature rose to 103° F. Further smears still showed no parasites, but quinine was given for three more days. He was subsequently afebrile, and at the time of discharge from the hospital on August 15, his spleen was at the costal margin and his erythrocyte count and hemoglobin concentration had risen to 4,370,000 and 14.7 gm. per 100 c.c., respectively.

The bloods of both parents were examined before and after the administration of adrenalin, but no malarial parasites were discovered. When the child was seen two months after discharge, he was free from symptoms except for slight chills. Quinine was given for two more weeks and further smears were found to be negative.

This child was an American-born boy of three years who had lived entirely in New York City. He received intramuscular blood from his father, who gave a history of malaria twenty-two and ten years previously. Two and one-half weeks after the injection he contracted quartan malaria. He was cured with quinine. Parasites could not be demonstrated in the father's blood.

CASE 5.—B. S. was a girl of Greek parentage, born in the United States. At the age of two years she first came to the Babies Hospital because of anemia, thus beginning a series of 13 admissions to the hospital and numerous clinic visits. The records kept during this period are voluminous, but unfortunately lacking in specific information concerning donors used in the 17 blood transfusions which she received. Consequently, although there is strong circumstantial evidence that malaria was transmitted to her through a transfusion, conclusive proof is lacking.

During the eight years in which she was followed, her presenting complaint was anemia, which showed all the characteristics of Cooley's erythroblastic anemia. An older brother died of severe anemia associated with splenomegaly. His spleen was removed just before death, and he had been transfused 15 times in all. B. S., the patient, had a large liver and spleen at the time of her first admission. Her hemoglobin was always low (3.7 to 7.4 gm. per 100 c.c.), and her erythrocyte count of commensurate level (1.0 to 2.5 million). The smears showed large numbers of erythroblasts. At first her leucocytes and platelets were within normal limits. The Wassermann reaction of the blood serum was negative and the fragility of the red blood cells normal. At the age of two and one-half years, splenectomy was performed, following which there was a tremendous increase in the platelet count and the number of erythroblasts appearing in the blood smear. Microscopic examination of the spleen showed distention of the sinuses with erythrocytes and a slight degree of pigment phagocytosis. There was nothing suggestive of malaria. During the latter part of her illness she acquired the mongoloid facies and roentgenologic bone changes characteristic of erythroblastic anemia.

Until her admission on April 21, 1928, she had received only two transfusions, both from her father. During this time, 28 blood smears were examined, and none showed malarial parasites. On the above date she was given a transfusion, probably from her mother. Although there is no specific statement that the mother acted as donor, there is a record of a compatible cross-matching between mother and daughter. Two days following transfusion she was discharged.

On June 25 she was readmitted because of weakness and increasing pallor. The next day she was given a direct transfusion from her father. On the following day,

quartan malarial parasites were found in her blood smear. Her temperature curve from the day of admission until July 20 was typical of quartan malaria with a spike to 102° to 104° F. every third day. On therapy of six drams of coco-quinine daily from July 18 until discharge on August 10, the parasites disappeared rapidly from her blood. A second direct transfusion from her father was given just before discharge. No mention is made in the record of any illness on the part of the father, who supplied the blood by the multiple syringe method at the height of her acute malaria.

For the next two and one-half years, she made sporadic visits to the clinic, apparently getting along fairly well without transfusion. Then between February, 1931, and November, 1932, she was admitted five times for transfusion, receiving seven from her father and three from her mother. There was never any febrile sequel other than an immediate reaction to the transfusion, and the numerous smears examined showed no parasites.

On Nov. 9, 1932, she was again admitted for transfusion and blood was given from her father on the following day. A second transfusion was given on November 22 because she had failed to respond with an adequate rise in hemoglobin. Soon after this, she contracted an upper respiratory infection followed by bronchitis and bronchopneumonia. On November 25 her temperature began to spike daily to 104° to 105° F. and a transient friction rub was heard over the precordium. On November 28 malarial parasites were seen again in her blood and quinine sulfate was started in doses of 0.6 gm. per day. This was continued for four weeks. After two days of quinine her temperature dropped sharply to normal and remained there. Malaria was regarded as an incidental finding rather than the chief cause of her acute illness. She was given another transfusion from her mother just before discharge.

On Jan. 19, 1933, she was admitted for the last time with lobar pneumonia, and died three days afterward. Autopsy confirmed the diagnoses of pneumonia and erythroblastic anemia. None of the organs revealed microscopic evidence of malaria.

This case is rather unsatisfactory because transfusions were not suspected as the cause of her malaria and no attempts were made to question or examine the donors. It is known that the child lived in New York City all her life, showed no malarial parasites in many blood smears, and then developed quartan malaria two months after receiving her first transfusion from her Greek mother. The source of her second malarial infection four and one-half years later is open to speculation since all the transfusions given during the preceding six months had been obtained from her father. Either this was a reactivation of the original infection which had become latent, or else her father, who was also born in Greece, may have been a carrier. The possibility of transmission from daughter to father during the direct transfusion at the height of her malaria cannot be excluded. It is interesting to note that ten transfusions from both parents were given during the four and one-half years in which she was free from malaria.

CASE 6.—G. E. first entered the Harriet Lane Home of the Johns Hopkins Hospital at the age of nine months because of a distended abdomen and difficulty in voiding. His father was Italian and lived in his native land until 1920. He remembered having attacks of chills and fever from time to time in Italy, and even since his emigration to the United States he had occasional aches and chilly sensations after a hard day's work. Since the birth of the patient, the family had been living in a suburb of Baltimore where there was no endemic malaria.

G. E.'s birth was normal, his feeding fairly adequate although low in vitamin D, and he had not been ill in any way before his admission to the hospital on March 31, 1932. During the week preceding his admission he had suffered from pain in his left ear, a distended abdomen, and occasional vomiting. His urinary output had

been small, voiding painful, and there had been long periods of urinary retention. These symptoms had prompted his local physician to perform a partial circumcision for relief of phimosis. Because there had been no relief of dysuria and abdominal distention, he was brought to the hospital.

The patient was a drowsy infant with dark skin, pale mucous membranes, and a temperature of 99.2° F. The left eardrum was perforated, but no discharge was present. The abdomen was rounded, tympanitic, and fairly tight. Peristalsis was audible. There was no evidence of free fluid in the peritoneal cavity and none of the organs was palpable. The penis was partially circumcised, and the glans and prepuce were red and swollen, with pus issuing from beneath the latter. The right testis and spermatic cord were enlarged but not tender. A blood count taken on admission showed 8.5 gm. of hemoglobin per 100 c.c., 5,300,000 erythrocytes, and 21,600 leucocytes, 79 per cent of which were polymorphonuclears. The smear showed achromia, anisocytosis, and poikilocytosis of the red blood cells, but no malarial parasites. The urine contained traces of acetone, diacetic acid, and albumin. A moderate number of white blood cells were seen on microscopic examination. The stools were loose, containing some mucus, but no blood or pus. The Wassermann reaction of the blood serum was negative.

The boy was thought to have a urinary tract infection in addition to the infection of his external genitalia. During the first three days in the hospital, his condition became worse. His temperature rose to 105° F. on April 2 and he was extremely ill, being delirious, irritable, and dehydrated. Little reason for this change could be gleaned from physical examination. A blood culture was sterile.

Because of his failure to improve, a transfusion was given on the next day, April 3. His father was used as the donor, and 125 c.c. of blood administered. There was improvement on the next day with a fall in the temperature to normal. He was catheterized and clear urine obtained, which contained a few red blood cells but no leucocytes. The voided specimens of urine continued to show several white blood cells on microscopic examination. On April 8 cystoscopy was performed and retrograde pyelograms obtained which showed no structural anomaly. Following this, the urine became bloody for several days and there was a brief bout of fever. On April 11, the spleen was palpated for the first time, and was described as firm. An abscess appeared on the right buttock, which was incised with the release of pus from which *B. coli* and alpha-hemolytic staphylococcus were cultivated. The irregular fever and pyuria, which had persisted until this time, now gradually disappeared until his discharge on May 8.

After the patient had been at home for a short time, his mother noticed recurring fever every third day. On the intervening days he seemed perfectly well. On May 23 she brought him to the dispensary because of this phenomenon. His temperature was 105° F. and his spleen was felt two fingerbreadths below the left costal margin. His urine was normal, and no pneumonia was apparent on fluoroscopic examination of the chest. The dispensary physicians were unable to account for his fever, and since he did not seem very ill, he was sent home.

Three days later, on May 26, the mother returned with the child, insisting that her previous story was correct. He was admitted to the hospital. Examination showed a temperature of 105° F., listlessness, flushed face, and rapid respirations. The abdomen was distended and both the liver and spleen were enlarged. The hemoglobin concentration was 10.2 gm. per 100 c.c., and the erythrocyte count 4,160,000. There were 11,000 leucocytes with 65 per cent polymorphonuclears. In the smear, segmented, presegmented, and ring forms of the quartan malarial parasite were seen in large numbers. There was anisocytosis and poikilocytosis of the red blood cells. The urine was normal.

Four hours after admission the patient's temperature dropped abruptly to normal. On May 28 many half-mature parasites were seen in the blood smear, including rosettes containing eight divisions, characteristic of *Plasmodium malariae*. On May 29 his temperature rose again to 105° F., without any chill, and in twelve hours it had fallen again to normal. Again on June 1, after two days of normal temperature, it spiked to 106° F. He was given 0.3 gm. of quinine dihydrochloride daily for twelve days and then 0.1 gm. per day. On June 5 the blood smear was free of parasites, and by June 10 there was a definite decrease in the size of the spleen. From this date on, his temperature remained normal until his discharge on June 17.

The father was examined, but his spleen could not be felt. Blood smears taken after the administration of adrenalin failed to reveal parasites. He was instructed to take quinine for two weeks, and was given two doses of neoarsphenamine.

G. E. was last seen on June 23, at which time he was still taking 0.1 gm. of quinine daily. He was asymptomatic and the spleen could be felt at the costal margin. He received two doses of sulpharsphenamine in addition to the quinine.

In summary, this patient was an infant of nine months, born near Baltimore of Greek and Italian parents. He received a transfusion from his father and developed quartan malaria in the ensuing six weeks. The malaria was easily controlled with quinine. The father had suffered with malaria more than twelve years previously and had had an occasional chilly sensation but no fever since. His spleen was not palpable and no parasites could be found in his blood. It might be added that this is the only case of quartan malaria recorded in the diagnostic files of the Harriet Lane Home.

DISCUSSION

The majority of single case reports have been made from regions in which malaria is not endemic, namely: the northern United States, France, Germany, Austria, Hungary, Spain, and Holland. As Wang and Lee[29] have pointed out, it is difficult in regions where malaria is commonly found to be sure that an infection following transfusion is not due either to mosquito transmission, or to relapse during the course of an acute illness, of a previously acquired latent malaria. Many of the authors mentioned above go into some detail to show that malaria is practically nonexistent in their localities, and stress the fact that their patients had neither previous symptoms of the disease nor exposure to it. In the experience of the Babies Hospital, there have been only five children besides the ones described above, in whom a diagnosis of malaria has been established during the last twenty years. Of these five, all but one gave a definite history of having contracted the disease in a foreign country or in the southern United States. Although tertian malaria is seen occasionally near Baltimore, the case reported from the Harriet Lane Home is the only one recorded in the diagnostic files in which quartan malaria was recognized. The exclusion of latent infections in my young patients is comparatively easy, since their entire lives had been spent in New York City. In adult patients, this point is more difficult to establish.

Where blood has been injected into newborn infants for the control of hemorrhagic disease or as prophylaxis against intracranial hemorrhage, the subsequent development of malaria may be interpreted as the flower-

ing of an infection transmitted through the placental circulation from an ante partum latent infection in the mother. The cases of Willetts, Epstein, and one of my own have been questioned on this ground. However, in 26 cases collected by Forbes,[30] either the congenital infection was manifest in the first three days of life, or the mother was suffering from symptoms of malaria during her pregnancy. This author does note two cases in which the mothers were asymptomatic and the infants remained well until the second month of life. In none of these is any mention made of blood injections.

In Table I and in the reports from the Peiping Union Medical College, it is obvious that there is not only a wide range in the length of the incubation periods, but also some variability in the infectivity of the donor for different, and even for the same recipients. In order to explain these inconsistencies, four variable factors must be taken into consideration: (1) the concentration of virulent malarial parasites circulating in the peripheral blood of the donor at the time of blood-letting; (2) the amount of blood injected into the recipient; (3) the degree of immunity present in the recipient; and (4) the directness with which the blood was transported from donor to recipient.

The number of parasites circulating in the donor's peripheral blood is almost always small, as witnessed by the common difficulty encountered in finding them in routine blood smears. Only half of the authors were able to find them in the donor at all, and several resorted to splenic massage, injections of adrenalin and strychnine, and thick smears before success was attained. Two factors are thought to be responsible for keeping the infection in the latent state. One is the tendency for all but a few of the parasites to remain in the spleen; the other is the high immunity of the host to his strain of parasite.

The injection of adrenalin is a time-honored method of increasing the number of parasites in the peripheral blood through contraction of the spleen. In the excitement and pain attendant upon blood donation, one might reasonably expect splenic contraction to take place, thus producing an increase in the infectivity of the donor's blood at the moment. Oehlecker's donor lends substantiation to this idea, since, although he had never had any symptoms of malaria, thirty-six hours after giving blood he had a chill and pain over the spleen. In addition, the mere withdrawal of a significant portion of the donor's blood volume is enough to stimulate splenic contraction. Since the donor's blood is not usually examined until a week or two has elapsed, it can be assumed that his spleen and parasites have had time to revert to their original state.

Nickum[31] describes the common usage of a hypodermic syringe by two morphine addicts, one of whom had latent malaria. The healthy addict contracted malaria after the first dose-splitting. After sharing the syringe a second time, the carrier also developed symptoms although he

had been completely free from them previously. This suggests that the virulence of the malarial strain was increased for the original host by passage through a nonimmune individual, so as to render the host's immunity insufficient to keep the infection latent.

When the number of circulating parasites in the donor's blood is small, it is quite obvious that the larger the quantity of blood administered, the greater will be the opportunity to introduce enough parasites to engender an active infection in the recipient. Transfusion thus preponderates over intramuscular injections in the tabulation, because of the larger volumes used. So too is it possible to explain the failure of my donor in Case 3 to infect a second recipient.

Complete natural immunity to tertian malaria has been encountered occasionally in attempts to induce malaria for therapeutic reasons.[32] Lesser degrees of such immunity may account in part for the longer incubation times which have been encountered, and for some instances in which some of several recipients from the same donor have escaped without infection. Under the comparatively standard conditions of experimental or therapeutic transmission, various authorities still give a wide range for the incubation period in each type of malaria, to wit:

Mühlens and Kirschbaum[33]:	Tertian	5 to 29 days
	Quartan	15 to 50 days
	Estivo-autumnal	7 to 14 days
Craig[34]:	Tertian (intravenously)	4 to 8 days
	Tertian (subcutaneously)	6 to 20 days
	Tertian (mosquito)	9 to 21 days
	Quartan (intravenously)	4 to 14 days
	Quartan (subcutaneously)	21 days
	Quartan (mosquito)	21 days
	Estivo-autumnal (intravenously)	4 to 5 days
	Estivo-autumnal (mosquito)	12 days
Joyeux[35]:	Tertian	5 to 31 days
	Quartan	12 to 50 days
	Estivo-autumnal	7 to 19 days
Ackermann and Filatov[36]:	Tertian	2 to 12 days

The consensus of opinion here favors a longer incubation period for *P. malariae*. In a general way this holds for the cases in Table I, but strict application is not possible.

The exact technique of transfusion probably plays some rôle in determining the length of the incubation period. Ackermann and Filatov[36] found that if citrated blood was allowed to stand before injection, not only was the incubation time prolonged, but after a period of four days, the blood failed entirely to induce malaria. Microscopic examination after four days showed the appearance of extracellular forms of schizonts, replacing the normal intracellular forms. As the period of standing was prolonged, both the intracellular and extracellular forms began to disappear. The authors recommend allowing the blood

to stand at least four days before use if there is any reason to suspect malaria in the donor. This of course is impractical in emergencies.

The three instances in which the person donating blood received malaria from the recipient could have been prevented if the indirect method of transfusion had been used instead of the direct method. The very short incubation period in Woolsey's case might have been due to the presence of a direct vascular communication between donor and recipient, but I should place more stress on the debility of the patient and his very low erythrocyte count (less than one million).

The infrequency of estivo-autumnal malaria in the series is striking. Gubb's patient, who was suffering an acute attack of malaria at the time of transfusion, is the only example of this type which I have found. On the other hand, the malaria seen among drug addicts has been predominantly of the estivo-autumnal type. This discrepancy is probably attributable to the fact that estivo-autumnal malaria is not so prone to exist in a latent, asymptomatic form. Where reliable histories could be obtained from the drug addicts, recent malarial symptoms were usually uncovered. The blood donors in most cases had been free from symptoms for several years.

Although five of the six cases which I am adding were of the quartan type, there is about an even division between quartan and tertian malaria in the series as a whole. The geographic origin of my donors probably explains this difference, as Greece and Italy are the two main foci.

Little attention has been paid to the treatment of the malarial carrier responsible for these accidents of transfusion. This neglect is probably justified because the carrier is asymptomatic and there is usually no possible way of recognizing whether or not he is responding to treatment.

Complete protection from malaria can be afforded to the recipients of therapeutic blood only by categorically excluding all donors who have ever inhabited districts in which malaria is prevalent. Neither history, physical examination, nor exhaustive blood studies will consistently unveil the malarial carrier. This policy has now been adopted by some professional donors' bureaus. Such exclusion is no hardship in the temperate zones, but is virtually impossible in malarial regions. Several prophylactic measures have been suggested for use whenever potentially infected donors must be accepted. Ackermann and Filatov, as noted above, advise a time interval of four to ten days between withdrawal and use of the blood. They found the addition of quinine to be without effect in forestalling infection. Pinard[26] reports a similar failure when mercurous cyanide was added to the citrated blood. Treatment of the donor with quinine before using him is likely to fail since most persons suffering from latent malaria are quinine-fast. The most rational suggestion is that the recipient be given quinine immediately following transfusion so as to destroy the parasites while small in number.

In Gubb's case alone, the induced malarial infection was severe. None of the other patients were acutely ill, and in all cases there was a prompt remission of symptoms when quinine was administered. Only one relapse was noted. Except for the experience of Wang and Lee, none of the authors felt that the convalescence of their patients was unduly hampered by the presence of malaria. Although such accidents are certainly to be avoided if possible, their infrequency and ready correction with quinine make it undesirable to resort to prolonged and complicated methods to exclude malaria in donors, especially in the presence of an emergency grave enough to warrant immediate transfusion. Of more importance to the physician is the knowledge that such accidents can occur, making him alert to the possibility of malaria when an unexplained fever follows a transfusion.

SUMMARY

1. Malaria may be transmitted by transfusion or intramuscular injection of blood from individuals suffering from latent, asymptomatic infections.

2. Twenty-three reports of this accident are analyzed.

3. Six new cases are added.

4. All but one of the 29 cases was of the tertian or quartan type.

5. The incubation period of clinical malaria following transfusion varied from one to fifty-six days, two-thirds of the cases occurring between the eighth and twenty-eighth days.

6. All cases responded to quinine therapy, only one suffering a relapse.

7. Less than half the donors had malarial parasites in their blood smears, and less than half had ever had symptoms of malaria; but all had at one time or other been in malarial districts.

8. Complete protection from this accident is possible only if all previous inhabitants of malarial regions are excluded as donors of blood or serum.

9. Judging by the number of reports, the accident is infrequent in temperate climates.

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PUBERTAS PRAECOX DUE TO DEXTROLATERAL GRANULOSA CELL TUMOR OF THE OVARY IN A FOUR-YEAR-OLD GIRL

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TUMORS play an important rôle as provokers of sexual precocity. It has been known for a long time that tumors of the corpus pineale, the suprarenals, and the genital glands are by no means rarely the cause of pubertas praecox. The present case is an example of the last type, i.e., a granulosa cell tumor in the right ovary of a four-year-old girl with distinct symptoms of pubertas praecox. This type of case is extremely rare, and only a few have been described in the works bearing on this topic. The reasons for reporting this case are as follows: First, it is a very early case. According to the report published by Bland and Goldstein in 1935, only 7 out of about 250 published cases of granulosa cell tumors have occurred in children under ten years of age, the youngest child being three years old. Second, the patient could be treated: after dextrolateral oophorectomy the symptoms disappeared, and after the operation the patient, during the time it has been possible to observe her, seems to have developed in a normal way. Finally, certain hormone biologic tests have been made, which may be of a certain interest in spite of the fact that they gave chiefly negative results.

CASE REPORT

M. Ö., a girl, was born Sept. 15, 1931. Diary 767/35. The birth weight was 3,200 gm., and she was breast fed. During the first three years development was apparently quite normal. No early illness.

About December, 1934, the child began to have a white, lacteal bad-smelling vaginal discharge. There were no complaints of pain or of difficulty in urination. The mother had always been in good health and had started menstruating when she was twelve years old. For some time she also had had a vaginal discharge, and both the mother and child in January, 1935, sought medical advice at St. Görans Hospital's out-patient department for cutaneous and sexual diseases, Stockholm, where the doctor precluded the possibility of gonorrhea and prescribed washing with moderately warm water. Both mother and child improved considerably, but the flow of the child never disappeared completely.

In the middle of September, 1935, at the age of four years, the patient had slight bleeding from the vulva for two days, staining the clothes somewhat. On the night of Oct. 25, 1935, there was similar but increased bleeding: three spots of penny size and two spots of halfpenny size were noted on the sheet. From then on small spots were constant, but smaller day after day. The day before the bleeding started the patient was obviously tired and went voluntarily to bed. There were no abdominal symptoms and no sickness.

From the Pediatric clinic of the Caroline Institute, Kronprinsessan Lovisas Vårdanstalt, Stockholm: director, Professor A. Lichtenstein.

The child seemed to have grown remarkably during the last half year. About a year ago she was one-half head shorter than a rather tall playmate of her own age but is now one-half head taller than the other girl. No absolute measures of length or weight had been taken.

The mother did not find that the child's psyche differed from that of other children of the same age. For about a year the mother observed that the breasts developed distinctly. No abnormal hairiness was observed, and no sexual abnormality was observed in the child's behavior.

The patient had always drunk a great deal, although it is difficult to get an idea of quantities. She has been particularly thirsty the last two years and perspires rather freely. Her appetite is good, and she sleeps well.

She was admitted to the Medical Department of Kronprinsessan Lovisas Vårdanstalt on Oct. 28, 1935.

Physical Examination.—Length, 117 cm. Weight, 26.7 kg. General condition not influenced. The first impression of the child was that of a miniature of a girl at the end of the age of puberty: The large mammas with areola and nipples well developed, the starting axillary and pubic hair and further the shy manner of the girl, during the examination and the "womanlike" expression of her face, all suggested that notion (Fig. 1). The general color of the skin was normal. Insignificant intertrigo was present in the right genitocrural fold and about the vulva. The skin felt obviously warm. Perspiration in the armpits was more than normal. The patient herself said that she felt cold.

Superficial lymphatic glands: Not abnormal. *Skeleton:* Head width, 52 cm. Breast width, 67 cm. Skeleton in other respects normal and well proportioned. Teeth, 10/10, fine. *Lungs:* No dullness. Vesicular breathing. No incidental sounds. *Heart:* Boundaries: left mammillary line—right sternal margin (8 + 2 cm.). Tones rich, pure. No accent or arrhythmia. *Abdomen:* Normal configuration. Limp, insensitive. Liver and spleen not palpable. No resistance.

Reflexes: Patellar reflexes a little marked bilaterally. Achilles tendon and abdominal reflexes normal. Chvôstek's and peroneal signs negative.

Throat: Diffusedly slightly red. Not furred. Tonsils rather big. *Eyes:* No abnormalities. Fundus oculorum show quite normal conditions.

Blood pressure: 120/80 mm. Hg.

External genitals: Both labia minora and majora a little bigger than normal. Clitoris—no remark. The mucous membrane red, mucus-furred. *Rectal Examination: Far back and to the right a soft resistance was felt with the tip of the forefinger. It was not possible to reach same bimanually. The consistency was limp and a little bumpy, and its size about that of a goose egg.* A smaller, harder resistance, probably the uterus, was felt further in the fore part.

Urine: Pale yellow, a little muddy. Reaction: acid. Albumin: negative. Reducing substance, negative. Sediment: none pathologic. The urine was analyzed for prolan with negative results. *Zondek-Aschheim's reaction, negative. Prolan test on mice according to Zondek: Less than 9 mouse units of prolan per liter of urine. Blood:* Hemoglobin 86 per cent (Autenrieth). Red blood cells, 4,400,000. White blood cells, 6,800.

Differential Count (Oct. 29, 1935)

Neutrophiles	Myelocytes	–
	Metamyelocytes	0.5%
	Band cells	5%
	Segment	65%
Shift to the left		5%
Eosinophiles		0.5%
Basophiles		–
Lymphocytes		27%
Monocytes		4%

Basal metabolism, according to Krogh, on Oct. 29, 1935, +22 per cent and on Nov. 4, 1935, +15.5 per cent.

Dextrose Tolerance Test

At 8:30 o'clock (Nov. 1, 1935) 266 gm. of 10 per cent glucose solution were taken. Body weight: 26.6 kg.

	TIME	BLOOD SUGAR MG. %	URINE C.C.	REDUCING SUBSTANCE
Fasting test before the trial	8:30	104	70	neg.
Test ½ hour after the trial	9:00	168		
Test 1 hour after the trial	9:30	114		
Test 1½ hours after the trial	10.00	150		
Test 2 hours after the trial	10.30	132	80	neg.
Test 2½ hours after the trial	11:00	108		
Test 3 hours after the trial	11:30	82	100	neg.
Test 3½ hours after the trial	12:00	100		
Test 4 hours after the trial	12:30	130		
Test 4½ hours after the trial	13:00	90		

Psyche: The patient struck one as being much older than she really was. Test of intelligence according to Binet-Simon test shows an intellectual age of five and one-half years.

Roentgen Analysis (Oct. 29, 1935) (Dr. Sahlstedt)

Radiogram of skull: Cranium of normal shape and thickness with rather distinct markings. Sutures and vessel furrows normal width. No intracranial calcification. Measurements of sella turcica 9 by 10 mm. No destructions provable.

Abdomen synopsis: Outline of abdominal wall and psoas muscles normal, alike on both sides. The right kidney is about 5 by 10 cm., the left kidney about 5.5 by 10.5 cm. The right kidney had normal shape; the left one showed a slight sinuosity of the outlines in its lower half. No calcifications perceptible within the abdomen. No pathologic shadows of soft parts perceptible within pelvis minor or the abdomen in general. Negative roentgen examination.

Abdomen synopsis (Oct. 30, 1935): Principally unchanged roentgen figure.

Urography (with 6 c.c. perabrodil i.v.): The excretion starts immediately on both sides. After applying compression normal-sized renal pelves are filled up with small calyces. No deformity or filling defect. No obstacle of passage perceptible within the ureters. The bladder was of ordinary shape and size. No deformity or filling defect perceptible. Negative roentgen examination.

Bones of hands and feet: The development corresponded to an age of at least six and one-half years, probably near nine years. *Bones of hands and feet* (April 2, 1936): No perceptible change of the development of the bones of hands and feet since last test. *Bones of hands* (Nov. 16, 1936): The development of the bones of hands as last test.

Length and Weight Figures

DATE	LENGTH (CM.)	WEIGHT (KG.)
Oct. 28, 1935	117	26.7
Nov. 19, 1935	118	24.7
Jan. 15, 1936	119	27.5
Nov. 18, 1936	123	29.0

On Nov. 4, 1935, the patient was transferred to the surgical department of the hospital for operation. On the indication: dextrolateral tumor of the ovary, the patient was operated upon the same day by Dr. E. Perman. He extirpated a dextro-

lateral ovarian tumor of the size of a tangerine with a tube of about the width of a pencil. The other ovary and tube as well as uterus, which seemed to be normally formed, showed a clear increase in size in relation to her age.

Since the operation the patient has been getting on very well. Menstruation has never begun anew. Psychically the child has changed in as much as she has regained the childish features characteristic for her age. She does not feel ashamed of being seen naked, the premature aspect of her behavior has abated a little. After the op-

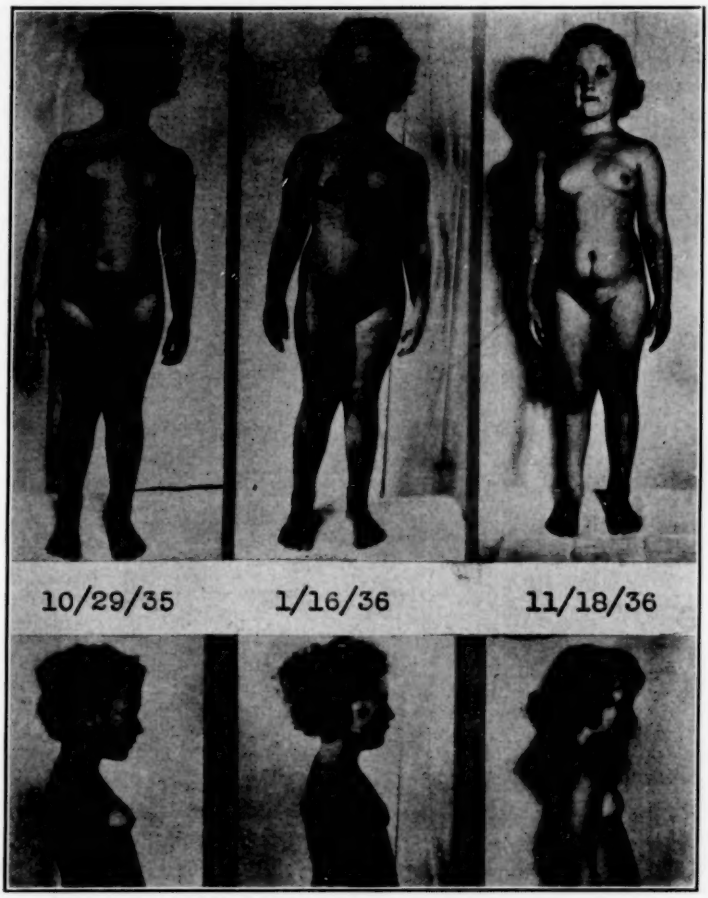

Fig. 1.—The patient before and after operation.

eration the patient has been checked repeatedly at the out-patient department, last time Nov. 20, 1936. The patient seemed then to be in perfect health. No bleeding, no vaginal discharge. The breasts, which were still pathologically overgrown, seemed, on the other hand, to have decreased considerably since the operation (Fig. 1).

Description of the Tumor.—The right ovary was transformed into a tumor of the size of a tangerine, about 7 cm. long. It was surrounded by a capsule without

perforation. When opened, it proved to consist of a small cystic tumor (Fig. 2). The main part having been taken care of for hormone biologic tests, the remainder was sent to the pathologic department of the Caroline Institute, where Professor F. Henschen delivered the following report:

"*Polycystic Granulosa Cell Tumor of Rather Typical Appearance.*—The tubular mucous membrane shows a well-developed papillary structure with multifid cylindrical epithelium."

Hormone Biologic Tests: With a small part of the preparation implantation was tried on infantile mice, about 0.1 gm. of the gland being implanted in the femoral muscles of each of four mice. On the fourth day after the implantation horn scales of typical appearance could be discovered in the vagina of one of the

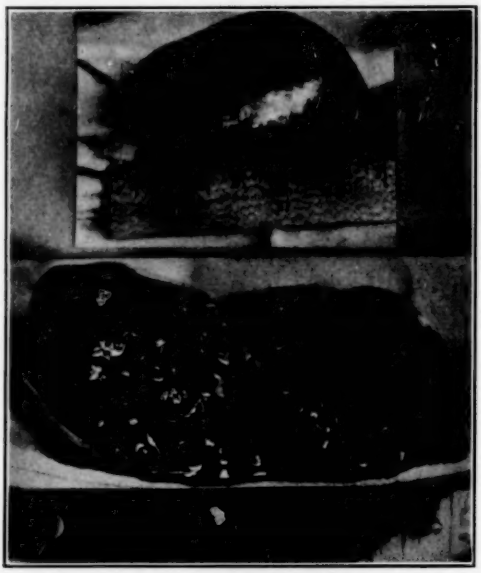

Fig. 2.—The tumor, above, unopened; below, cut up.

mice, i.e., the infantile mouse had reached her period of heat (estrus). *It had thus proved that the tumor in question contained folliculin in greater or smaller quantity.*

The remainder of the tumor was treated with alcohol with the object of extracting existing sex hormones according to the procedure indicated by Zondek. But, although Zondek's procedure was observed as strictly as possible, the obtained extract proved to be absolutely ineffective: injection of same in both uncastrated and castrated mice gave in all cases negative result.

At the examination of the patient thirteen months after the operation there were no signs of relapse. The prognosis of the case is thus probably good, although it is not possible to be quite positive about it. In the case related by Bland and Goldstein (seven-year-old girl) the patient was free of symptoms for eighteen months after the first operation, when menstruation began anew and the cause was discovered to be a granulosa cell tumor in the other ovary. It was necessary to extirpate the second tumor.

DISCUSSION

The case is one of pubertas praecox in a four-year-old girl, who, besides the advent of menstruation and appearance of clear secondary sexual distinguishing marks, also showed increased growth in length and early ossification of the bones. The etiology of this disturbance in the present case was a dextrolateral granulosa cell tumor of the ovary.

The chief interest of a case of this kind is, of course, combined with the result of the test on the tumor's possible contents of sexual hormones. In the earlier cases there has been very little done in this respect, and the reports vary greatly. Of interest is Pahl's statement about positive Zondek-Aschheim's reaction (H.V.R. III) in a similar case. Pahl himself is rather uncertain because only one of the four animals examined gave positive results and the reaction always became negative on later occasions. In the case of Bland and Goldstein (seven-year-old girl) the Zondek-Aschheim reaction was negative in the first instance, but at the relapse it became positive and the percentage of folliculin in the blood was also increased. It is thus evident that in certain cases of granulosa cell tumor with pubertas praecox there is a considerably increased quantity of folliculin in the urine and the blood of the patient and further a quantity of prolan that is normally met with only in pregnancy.

In the present case, however, the Zondek-Aschheim reaction was negative, and the percentage of prolan in the urine of the patient at any rate was extremely insignificant (less than 9 mouse units per liter). An analysis regarding the contents of sex hormones in the granulosa cell tumor has been made in the present case, in as much as 0.1 gm. of the gland was implanted in the femoral muscles of mice, which gave the result that one of the animals reacted positively. *This may be evidence of the fact that the tumor in question contained folliculin in greater or smaller quantity.*

Finally the patient showed, as stated above, in addition to pubertas praecox an increased growth in length and premature ossification of the osseous centers of hands and feet. On the whole, it is not known if the rapid growth in length during the age of puberty is the result only of increased ovarian activity, or if in addition hormones from other endocrine glands play important rôles.

On the other hand, it seems probable that the hormone excretion from the granulosa cell tumor (leaving aside the question if it has only been a case of folliculin or if possibly other hormones have been at hand) in this case has played an important rôle not only for the development of the secondary sexual distinguishing marks, but also for the rapid growth of the bones during that period. This belief is also proved to some extent by the fact that the development of the bones after the extirpation of the tumor, at renewed examination more than a year after the operation, do not seem to have proceeded any further.

In order to make a thorough research on the hormones of the granulosa cell tumor, preparation had been made for a series of tests on animals with extract from the tumor. Unfortunately these could not be accomplished because, as stated above, it proved to be impossible to produce an effective extract.

In the works bearing on this topic there are only vague references made to the direct influence of folliculin on the development of the bones. Trials on animals with a view of penetrating further into that problem would no doubt be of great interest.

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ACUTE HEMOLYTIC ANEMIA (LEDERER TYPE)

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IN 1925 three cases of rapidly developing anemia of a previously undescribed type were reported by Lederer.[1] The outstanding features of these cases were: acuteness of onset, evidence of rapid erythrocyte destruction, marked bone marrow regeneration, recovery following transfusion, and the absence of sequelae. Again in 1930 he[2] reported three additional cases and cited Holst and Christiansen as each reporting a typical case. Parsons[3] in 1931 reported four cases and in 1933[4] five additional ones.

Recently it was our privilege to see a case which conformed clinically and hematologically with the cases of acute hemolytic anemia originally described by Lederer, and we believe that the rarity of this condition justifies its recording in the literature.

CASE REPORT

E. T., a white female, aged seven years, of German and English extraction, was admitted to the Childrens Hospital on March 2, 1937, with the chief complaints of headache, dizziness, inability to see, and vomiting. The birth and developmental history were essentially normal. There was a history of mumps at five years of age and tonsillitis on two occasions prior to a tonsillectomy at five and one-half years of age. From the age of two years to six years, the patient had frequent attacks of urticaria associated with abdominal pain and vomiting, following the ingestion of food. The particular articles of diet that provoked these attacks were not ascertainable. There was no history of the ingestion of any known hemolytic agent. The family history was negative except that the father had three attacks of purpura hemorrhagica before puberty. Examination of the parents' blood revealed no abnormalities. The patient had been perfectly well until two weeks prior to admission when she developed a respiratory infection and was kept in bed for one week. She returned to school apparently well except for a slight residual cough. Two days prior to admission the mother noted listlessness and pallor. The patient complained at this time of frontal headache and dizziness, and vomited on two occasions. Her condition remained unchanged until about six hours prior to admission, when there was a sudden increase in all signs and symptoms together with extreme restlessness and inability to see.

On admission the patient was critically ill, stuporous, and dyspneic. Temperature was 103.8° F., pulse 132, respirations 40 per minute. The skin and sclerae had an icteric tinge. Mucous membranes were pale. No rash or purpuric spots were present. Eyegrounds were negative. The heart by percussion was slightly enlarged to the left, and a hemic murmur was present at the apex. The liver was palpable two cm. below the costal margin. The spleen was palpable

From the Childrens Hospital and the Division of Pediatrics, the Department of Medicine, Ohio State University.

TABLE I

	ERYTHROCYTES (MILLIONS)	HEMOGLOBIN—GM./100 C.C. (NEWCOMER)	COLOR INDEX	VOLUME INDEX	HEMATOCRIT	RETICULOCYTES PER CENT	NORMOBLASTS PER 100 W.B.C.	MEGALOBLASTS PER 100 W.B.C.	ANISOCYTOSIS	POIKILOCYTOSIS	PLATELETS (THOUSANDS)	W.B.C. (THOUSANDS) CORRECTED	P.M. NEUTROPHILES	P.M. EOSINOPHILES	P.M. BASOPHILES	MYELOCYTES	LYMPHOCYTES	MONOCYTES	ICTERUS INDEX	ERYTHROCYTE RESISTANCE
March 2, 1937	0.95	3.6	1.05			1.5	1	1	++	+		33.5	84	1		4	10	1		
3 10 A.M.	1.09	4.6	1.24	1.17	11.5	5.2	3		++	+	658.0	18.5	71	1	2	8	13	5	50	Norm.
4 P.M.	1.10	2.6	0.68				3	1	++	+		29.8	89			1	10			
4	1.05	2.1	0.57				5	2	++	+		20.2	74	1	1	3	21			
5	1.28	3.7	0.86				5	2	+++	++		26.0	82	1		3	14			
6	1.06	2.4	0.67				5	3	+++	++		22.2	78	1		3	18			
8 10 A.M.	1.60	5.9	1.09									9.3	84		1	1	14			
2 P.M.	1.58			0.99	14.0	15.0	31		+++	++	657.0	13.3	53	5		6	35	1	25	Iner.
9	1.40	5.2	1.10				5	4	+++	++		10.9	64	1		1	34			
10	1.49	5.0	1.07				4	1	+++	++		10.3	68	1		1	30			
11	1.27	5.4	1.28				2	2	++++	++		12.3	54	2		1	43			
13	1.34	4.9	1.08				4	2	++++	+++		8.7	84	2		1	13			
16 10 A.M.	1.44	4.6	0.94				5	3	++++	+++		9.2	72			1	27			
3 P.M.	1.57	5.7	1.08			19.6	5		++++	+++	703.0	11.0	55	3		10	32		25	Iner.
18	1.50	5.2	1.03				5	2	++++	+++		10.3	79	2		1	18			
20	1.71	5.4	0.94				2	1	+++	+++		6.6	66	3		1	30			
22 8 A.M.	1.63	6.5	1.17				1		+++	+++		5.4	73	3			24			
2 P.M.	1.82	7.6	1.24			24.8	2		+++	+++	182.0	7.2	65	3	2	2	25	3	20	
24	1.84	7.0	1.11				1		+++	++		4.7	71	4			25			
April 5, 1937	3.67	13.1	1.05	1.18	39.0	4.4			+	+	350.0	5.7	44	7		1	41	6		Norm.

five cm. below the left costal margin. No other abnormalities were noted. Wassermann, Kahn, and tuberculin tests were negative. Blood culture was sterile. Roentgenograms of the chest were negative except for slight cardiac enlargement to the left. Sinus roentgenograms were negative. The urine was straw-colored, clear, and negative for sugar, albumin, casts, red and white cells. No chemical tests were done for hemoglobinuria or increased urobilin. Stools were of normal color and consistency. No examination was made for ova or parasites. The blood count was as follows: Red blood cells 950,000, hemoglobin (Newcomer) 3.6 gm., white blood cells 33,500. The differential count was polymorphonuclears 82, myelocytes 3, lymphocytes 14, monocytes 1. No sickling of the erythrocytes was noted in the moist film studies at any time.

In view of the critical condition and the marked anemia, a transfusion of 200 c.c. of citrated blood was given with no apparent benefit. Twelve hours later another transfusion of 150 c.c. of citrated blood was given. For three days the patient's condition remained critical, with delirium, extreme restlessness, and vomiting being noted. The patient complained of dizziness and occasional pain

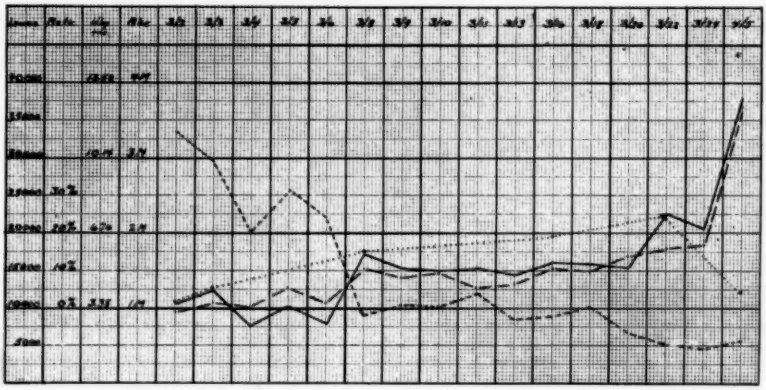

Fig. 1.—Erythrocytes .....; hemoglobin—; reticulocyte .....; leucocytes -----.

in the upper left quadrant. On the fourth hospital day a transfusion of 400 c.c. of citrated blood was given. Following this, an immediate improvement was noted in the patient's condition. Liver extract and ferric ammonium citrate were started on the fifth day. Admission temperature was 103.8° F., followed by daily fluctuations reaching 101° to 102° F. until the eighteenth day, when it became normal. The splenic tumor was present on all occasions, although it was just palpable at discharge on the twenty-third day. The icteric tint and hemic murmur persisted throughout hospitalization. However, on the twelfth day following discharge, these signs had disappeared. The patient was greatly improved and had no complaints. The blood picture at this time (April 5, 1937) was as follows: red blood cells 3,670,000, hemoglobin (Newcomer) 13.1 gm., color index 1.05, volume index 1.18, hematocrit 39, reticulocytes 4.4 per cent, slight anisocytosis and poikilocytosis, platelets 350,000, white blood cells 5,700, differential count: polymorphonuclears 44, eosinophiles 7, myelocytes 1, lymphocytes 41, monocytes 6. No nucleated red blood cells were present. The erythrocyte fragility was of normal resistance. At one, two, three, four, and five months following discharge the patient was entirely well and presented normal blood pictures.

TABLE II

ADMISSION CLINICAL AND HEMATOLOGIC FINDINGS	LEDERER'S CASES[1, 2]						CASE PRESENTED
	CASE I	CASE II	CASE III	CASE IV	CASE V	CASE VI	
Age	19 yr.	16 mo.	35 yr.	24 yr.	3 yr.	6 mo.	7 yr.
Sex	M.	M.	F.	M.	M.	M.	F.
Onset	3 days	3 days	6 days	3 days	2 days	6 days	2 days (?)
Fever	+	+	+	+	+	+	+
Icterus	+	+	+	+	+	+	+
Pallor	+	+	+	+	+	+	+
Weakness	+	+	+	+	+	+	+
Vomiting	0	0	+	+	+	+	+
Diarrhea	0	+	0	0	0	0	0
Abdominal pain	0	0	0	0	+	0	+
Backache	0	0	+	0	0	0	0
Headache	+	0	+	0	0	0	+
Splenomegaly	+	+	0	+	0	+	+
Hepatomegaly	+	0	+	0	0	0	+
Treatment	Transfusion	Transfusion	Transfusion	Transfusion	Transfusion	Transfusion	Liver and Transfusion
Outcome	Recovered	Recovered	Recovered	Recovered	Recovered	Recovered	Recovered
Erythrocytes (millions)	1.99	0.96	0.78	3.12	1.07	0.95	0.95 (Newcomer)
Hemoglobin (Dare)	43%	20%	14%	50%	10%	20%	21%
Color index	1.10	1.04	0.95	0.80	0.50	1.00	1.05
Normoblasts	+	+	+	+	+	+	+
Megaloblasts	+	+	+	+		+	+
Leukocytes (thousands)	33.6	52.0	37.0	29.0	39.6	20.0	33.5
Platelets (thousands)	210.0		150.0			275.0	686.0
Hemolysis	+	+	+	+	+	+	+

The changes in the blood picture are shown in Fig. 1 and Table I. A marked anemia of hyperchromic type was noted on admission. On the second, third, fourth, and fifth days the anemia was of a hypochromic type, after which the hyperchromic picture again predominated. A moderate degree of anisocytosis and poikilocytosis was present on admission which later became marked. Macrocytosis was present on all occasions. A Price-Jones curve was not obtained. The fragility test was either normal or showed increased resistance on all occasions. The icterus index was elevated at the first examination and gradually declined. Bone marrow activity was evidenced by a marked degree of immaturity of the erythrocytes. Nucleated red cells were present on admission and reached the highest peak on the sixth day. The reticulocyte response was marked, rising from 1.5 per cent on admission to 24.8 per cent on the twenty-first day. Two weeks later it had fallen to 4.4 per cent. The hematocrit rose from 11.5 on March 3, 1937 to 39.0 on April 5, 1937. Both erythrocytes and leukocytes showed stimulatory response. There was no depression of thrombocytes. The leucocyte count was corrected after the method of Lederer[1] (who stated that the leucocyte count as estimated in the usual way is erroneous in the presence of great numbers of erythroblasts). The correction was made by subtracting the erythroblasts as estimated in the stained and "vital" preparations from the total leucocyte count. Table II shows the similarities of Lederer's cases and the case presented.

COMMENTS

In attempting to classify this syndrome one meets with various opinions. Josephs[5] places acute hemolytic anemia in the hemolytic-erythroblastic group; he characterizes the cases belonging to this group by: great reduction of red cells as well as hemoglobin, increased blood destruction, changes in the blood indicating increased regeneration, often the presence in the blood stream of immature cells, and in some cases, especially the more severe ones, evidence of "hypoplastic" reaction. He subdivides the hemolytic-erythroblastic group as follows: I. Those cases dependent primarily on constitutional factors, in which are included congenital hemolytic icterus, sickle cell anemia, and Mediterranean anemia (Cooley). II. Chronic cases dependent primarily on extrinsic factors, III. Acute hemolytic anemia. Parsons[4] gives the following classification (erythronoclastic anemias): I. Acute hemolytic anemia (Lederer type), II. Subacute hemolytic anemia, III. Von Jaksch's syndrome (subchronic hemolytic anemia), IV. Acholuric jaundice.

Various etiologic factors[5]—infection, intoxication, and allergy—have been advanced as the cause of acute hemolytic anemia. Lederer[1] states, "the behavior suggests an infection with selective action concentrated on the reticulo-endothelial system." All of Lederer's cases in children showed gastrointestinal symptoms as did our case. Some of Parsons'[4] cases in children, however, did not show gastrointestinal symptoms and he concluded, "if these cases are infective in origin, the infection is not necessarily intestinal." He further stated "the picture suggests that the illness is the result of some infection but like all other writers on this subject we have been unable to discover the infecting agent." In

the case presented, while there was no positive evidence of infection, there was, however, a definite history of antecedent respiratory disease. On admission the patient presented a clinical picture suggestive of an acute infection with high fever, marked toxemia, splenomegaly, and leucocytosis. Symptoms referable to the gastro-intestinal system consisted of pain in the left upper quadrant and vomiting.

Josephs[5] suggests that some form of allergy may have been a factor in the cases of acute hemolytic anemia reported by Waltner in 1930, by Williams in 1933, and in the case of acute hemolytic anemia reported by Sylvan in 1933. "Favism,"[5] a form of acute hemolytic anemia occurring in Italy, follows the ingestion of raw fava bean and occasionally from passing a field in which the bean is growing. The attack is evidently allergic. Whether or not there was an allergic factor in the case under discussion, we can only surmise, but it is interesting to note that during the period between the second and sixth year of age the patient had frequent attacks of urticaria, abdominal pain, and vomiting, following the ingestion of food. During the first three days of hospitalization there was occasional pain in the upper left quadrant and also vomiting, although there was no apparent relationship between these two symptoms. There was no evidence of urticaria or eosinophilia. No tests for allergy were done.

SUMMARY AND CONCLUSIONS

1. A case of acute hemolytic anemia with sudden onset, prostration, fever, leucocytosis, and rapidly developing anemia is described.
2. There was evidence of rapid destruction of blood and of bone marrow regeneration.
3. Infection and allergy are considered as causative factors.
4. Transfusions of 350 c.c. of citrated blood during the first twelve hours and 400 c.c. of citrated blood on the fourth day were given. Complete recovery followed the transfusions.
5. This case conforms clinically and hematologically with the cases described by Lederer.[1, 2]

We wish to acknowledge our indebtedness to Dr. C. A. Doan and Dr. C. V. Moore of the Department of Medicine of the Ohio State University College of Medicine for their assistance in the management of this case.

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ENTEROGENOUS CYST OF THE DUODENUM SIMULATING PYLORIC STENOSIS

Report of a Case in an Infant With Recovery Following Gastroenterostomy

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THERE have been only seven cases of enterogenous cysts of the duodenum described to date. This is the first case that has come under our observation at the St. Louis Children's Hospital. It is felt that more attention should be directed to so rare a condition, and it is with this in mind that the following case is reported.

L. D., a four-week-old white girl, was admitted to the St. Louis Children's Hospital on Dec. 12, 1936, with the complaint of vomiting and loss of weight for two and a half weeks. The child was born Nov. 11, 1936 after a prolonged labor of three days. Forceps were used and a slight bruising of the face and scalp ensued. Artificial respiration was necessary for resuscitation. The birth weight was 7 pounds, 2 ounces, and the child was put on breast feedings every three hours. The day following the delivery, dark red blood was noted in the stools, which disappeared after intramuscular injection of whole blood. According to the family, the child did extremely well until the eleventh day of life; at this time she began to vomit. At times the vomiting was nasal and projectile. The vomitus was at no time bile-stained. The stools were small but occurred daily. There was, however, definite weight loss, which continued for two and a half weeks. Before admittance to the hospital the infant had been weaned from the breast and put on an artificial formula.

Physical examination revealed a white child who looked acutely ill. There was a severe degree of dehydration and malnutrition. The child weighed only 2,500 grams. The temperature was 37.8 degrees C. The right tympanic membrane was injected and the left was full with a loss of the normal landmarks. The abdomen was scaphoid. There were no gastric waves visible. A freely movable tumor, about 2 to 3 cm. in diameter, was easily felt. It was rounded and no tenderness was elicited. Everyone who felt the tumor remarked: "This is the largest pyloric tumor I've ever felt." The fingers and toes were long and slender, enough to suggest the possibility of arachnodactylia. The Wassermann reaction was negative. Urinalysis revealed nothing abnormal. Examination of the blood revealed 75 per cent hemoglobin (Sahli), red blood cell count 4,060,000 per cubic centimeter, 17,000 white blood cells, with a Schilling differential count as follows:

	B	E	M	J	St	S	L	Mon
%	0	0	0	1	27	63	15	4

There was no change in the size and shape of the red blood cells. The platelets were normal. A diagnosis of hypertrophic pyloric stenosis, acute bilateral otitis media, dehydration, and arachnodactylia was made.

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Upon admission the serum carbon dioxide content was 67.5 volumes per cent, and the sodium chloride 566 milligrams per cent. Four hundred cubic centimeters of lactate-Ringer's solution were given subcutaneously. An opaque feeding could still be seen in the stomach at the end of seven hours. The child was prepared for operation by intravenous injection of 10 per cent dextrose and citrated blood, and subcutaneous injection of lactate-Ringer's solution. The operation was decided upon at this time as the parenteral fluids had relieved the dehydration and corrected the chemical changes. The left ear drum which previously had been bulging seemed to be subsiding.

On Dec. 13, 1936, the abdomen was explored by Dr. Robert Elman. The pylorus was exposed, revealing a large tumor, cystic in nature. It extended from the pylorus for a distance of 2 to 3 cm. along the duodenum, occupying apparently the anterior wall of the duodenum. The contents of the cyst were evacuated with a small hypodermic needle. About 15 to 20 c.c. of straw colored fluid were obtained. It was slightly mucilaginous in character but obviously contained no intestinal contents as the fluid was crystal clear. After aspiration, a number of nodules were palpable along the margin of the cyst. One of these nodules was partially removed for biopsy. The cyst fluid revealed a carbon dioxide content of 54.5 volumes per cent. It was alkaline to phenolphthalein. There was no amylase present. The biopsy showed bits of loose connective tissue with small young fibroblasts scattered throughout. The question of excision of the cyst, of marsupialization, or gastroenterostomy was considered, but in view of the infant's poor condition and of the fact that the obstruction was definitely relieved after evacuation of the cyst, it was decided to do nothing further. The possibility of the fluids containing digestive ferments and the danger of entering the duodenal lumen helped make this decision. The baby was returned to the ward in good condition. A formula of one part evaporated milk, one part 1 per cent lactic acid, one part water with 5 per cent Karo was fed six times daily in amounts of three ounces at a feeding. There was no vomiting the next day, but on the second postoperative day vomiting recurred and became steadily more severe.

The tumor again became palpable seven days after the first laparotomy on Dec. 20, 1936. The abdomen was again opened on this day. It was found that the cyst had refilled. After evacuation of a more turbid mucoid material, an attempt was made to find a line of cleavage which might enable enucleation of the cyst. The tumor, however, seemed to merge gradually with the wall of the duodenum, and it seemed that any attempt at removal would undoubtedly lead to a perforation of the gut and perhaps necessitate a resection of the entire wall. It was therefore decided to do a gastroenterostomy which was easily performed after making an opening in the mesocolon and stitching its edges to the posterior wall of the stomach. The anastomosis was made between the posterior wall of the stomach and the jejunum just beyond the ligament of Treitz. Fine silk was used for the outside row and catgut for the inside layer. It was felt that the feedings should be instituted immediately instead of waiting the usual three to four days because of the poor nutrition. The infant was started on equal parts of milk, water, and 20 per cent buffer solution, 15 c.c. being given every four hours alternated with 10 per cent buffer solution. The feedings were increased 15 c.c. daily until the baby received three ounces at a feeding when the usual lactic acid formula was started. From this time on the child did well. There was no further vomiting. The baby was discharged from the hospital on Jan. 7, 1937, weighing 3,050 grams, an increase of 500 grams over the admission weight.

The patient was seen May 24, 1937, at which time her weight was 17½ pounds. She was then six months old and had not vomited since her discharge from the

hospital. Her abdomen was soft and no tumor mass could be felt. An opaque feeding was found still to leave the stomach through the opening made by the gastroenterostomy.

According to the recent correspondence, Nov. 4, 1937, the patient was in excellent health. She is at present a year old and weighs 24 pounds. She has not vomited since her discharge from the hospital. There has been no tendency toward constipation, nor has any excess enlargement of the abdomen been noted.

REVIEW OF THE LITERATURE

Gardner and Hart[1] in 1935 reported the case of a fifteen-year-old white girl who had frequent attacks of abdominal pain and vomiting. In the past history was the fact that at the age of two years she had an attack of unexplained hematemesis and melena. When she was examined at the age of fifteen years, a moderately tender mass was felt in the gallbladder region, which was about 10 cm. in diameter. An exploratory laparotomy revealed a distended cystic mass in the upper third of the duodenum. This could not be emptied into either the duodenum or stomach. The stomach was opened, the interior inspected and the cystic mass seemed to lie within the duodenal wall. The cyst was aspirated and a thin, clear, slightly greenish fluid was obtained. An anastomosis was made between the cyst and the duodenal lumen. The patient had an uneventful recovery.

Smith[2] reported a case in 1930 of a two-week-old female infant who had vomited after practically every feeding since birth. A tumor was felt at the pyloric region and a diagnosis of hypertrophic pyloric stenosis was made. Operation revealed a cyst in the anterior wall of the duodenum. There was no communication between the cyst and the duodenum. The cyst was drained externally. The child died one week later.

Maddox[3] reported a case in 1927 of a three-month-old baby who had vomited following feedings. A mass was palpable in the pyloric region. At operation the first portion of the duodenum ended in a large cystic tumor. The child's condition was too poor to permit further operation, and it died sixteen hours later.

Another case of a nineteen-day-old female with persistent vomiting was reported by Waugh[4] in 1923. A large cyst was found at operation that was connected with the posterior wall of the duodenum. The cyst was drained and the child did well for six weeks. The cyst refilled and the baby died of pneumonia one week after a second operation.

In 1919 Meyer[5] reported a three-week-old female who began to vomit when thirteen days old. The child died before any surgical intervention could be attempted. Autopsy revealed a cyst the size of a hen's egg on the medial wall of the duodenum.

A newborn male infant who died immediately after delivery was reported by Roth[6] in 1881. The abdomen was dome-shaped and contained a large cyst arising from the wall of the duodenum. There was no communication between the cyst and the lumen of the duodenum.

Sanger and Klopp[7] in 1880 reported a newborn child who died during delivery. There were five cysts in the abdomen, three from the intestines and one arising from the duodenum.

COMMENT

Despite the fact that there has been no case described in which the diagnosis had been made before operation, we feel that we should have been suspicious that the pyloric obstruction was due to something other than the usual hypertrophic muscle, as the tumor was so easily felt and was somewhat larger than the usual pyloric tumor. Except for the case which we are reporting, the few infants operated upon for a similar condition have failed to survive.

Perhaps the successful outcome of our case was due in part to the nursing care which she received. Because of the prevalence of influenza, it was thought imperative to isolate her in the premature infant room, and care for her with special nurses. Preoperative and postoperative parenteral fluid therapy, as well as the method of feeding must, of course, also have played a part in the successful outcome.

The diagnosis of hypertrophic pyloric stenosis had been made in the majority of cases. All the cases of duodenal cysts were infants except the one described by Gardner and Hart.[1]

SUMMARY

An enterogenous cyst of the duodenum in a four-week-old baby was treated successfully by gastrojejunostomy. The only other successfully treated case reported in the literature was that of a girl operated on at the age of fifteen years.

Altogether eight cases have been described, five of these occurring in females and one in a male. In two cases the sex was not recorded.

The clinical manifestations are usually those of pyloric obstruction.

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ENCOPRESIS IN CHILDREN

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ENCOPRESIS is defined by Kanner[1] as "the act of involuntary defecation which is not directly due to organic illness." The term was suggested in 1926 by Weissenberg,[2] who considered the condition to be analogous to enuresis. The term fecal incontinence is now reserved for soiling which is caused by organic lesions such as abnormalities of the rectum or anal sphincter, cerebral or spinal diseases or injuries, and infectious or toxic conditions in which there is general weakness, delirium, or stupor. A diagnosis of encopresis is not made, therefore, until organic causes are, as far as possible, ruled out.

HISTORICAL

It has long been known that involuntary defecation for which no organic cause can be found occasionally occurs in children. Fowler[3] reported 2 cases in 1882. One, a seven-year-old boy "of mushroom growth and hothouse culture," because of excessive study under pressure, "developed into a sort of loaded phonograph, capable of starting automatic expressions which afforded much entertainment to visitors, and gave the ambitious father great hope and comfort. Under such conditions," the author stated, "it is not to be wondered at that something gave way, and fortunately for the brain, it was the sphincter ani." Cessation of punishment and relief from study resulted in discontinuance of the almost daily involuntary discharges in about three weeks. The other case was that of a thirteen-year-old girl who had "befouled herself" nearly every day since infancy. Ergot, strychnine, and tonics were followed by recovery. Fowler considered ergot to be a specific cure in these cases, as in enuresis, because of its "contractile effects upon the vessels of the cord" and "its established value as a restorative of contractile power to muscle."

In 1905 Ostheimer,[4] having seen 3 boys with soiling in a period of six months, reviewed the literature and was able to find only 12 cases. Five of these children, however, had either general or local organic conditions. In 3 cases the soiling was associated with severe constipation. In one of Ostheimer's cases there was a vesicle calculus.

Goodhart and Still[5] stated in 1905 that this condition "is nearly always associated with peculiarities of mental action, which indicate that the treatment should be moral rather than physical. For instance, al-

From the Psychiatric Clinic of The Harriet Lane Home for Invalid Children, Johns Hopkins Hospital, Baltimore, Md.

though these children are quite sane, one may be subject to outbursts of passion, another will be unduly timid, another will be quite insensible to pain, another may be sullen; in all, in fact, if inquiry be carefully made as to home behavior, there is some unnatural mental trait which shows that we are dealing with some of the milder forms of mental instability. Our experience has not led us to think highly of local treatment in these cases; they do well under kind but firm moral control; it is best to send them away from home to a small school, and in most cases the condition disappears."

In 1923 Morichau-Beauchant[6] described a number of cases with what he called "paragenital autoerotism." It was his opinion that the "pseudo-incontinence" is a survival of the autoerotism of the infant, and that children hold back their stools because of the pleasurable sensation from the excitation of the mucous membrane of the anus until the imperious demands of nature intervene.

According to Pearson,[7] "training methods may be unsuccessful for much longer than the usual time because the child is of the constitutional type which gets much pleasure from bowel activities." "In many cases," he further stated, "there is definite evidence of lack of parental love for the child," and "the soiling becomes a method of attracting the parents' attention and of spiting them."

Hendrick,[8] an exponent of the Freudian viewpoint, stated that after the oralerotic stage of the "pregenital psychosexuality," the child's "anus supplants the mouth as the chief source of sensual pleasure. Its use, however, is soon much limited by toilet training, and his resentment of this frustration of his pleasure is expressed in phantasies in which defecation represents definite aggression and destruction of the hated one."

Pototzky[9] reported an eleven-year-old boy whose trousers were found filled with feces about an hour after each scolding by his parents. He delighted in their embarrassment and disgust which was caused by their handling of his soiled clothing.

Thom[10] mentioned a seven-year-old girl who reacted to a jealousy situation not only by encopresis but also by smearing with her feces the walls of her room, her clean linen, and her dishes and food. He stated that "one can only say that these cases call for a careful psychiatric examination by the best qualified person available. And it will often test all of his skill and ingenuity to understand the mental processes at work that result in such conduct."

REVIEW OF 70 CASES

Because of the scant attention which is given in the pediatric literature to this condition, it seemed worthwhile to review the cases of encopresis which have been seen in the Psychiatric Clinic of the Harriet

Lane Home for Invalid Children. From Nov. 1, 1930 to March 11, 1937, 2,406 children under fifteen years of age were examined; of these 70 were encopretic. This is an incidence of 2.91 per cent or 1 to every 34.36 patients. In this group encopresis was about one-tenth as frequent as enuresis. It is interesting to compare this frequency with that found in the Maryland State Mental Hygiene Clinics where in 1936 soiling was a complaint in only 5 of 469 cases, 373 of whom were under fifteen years of age. All of the 70 encopretic children, before being seen in the psychiatric clinic, were given physical examinations in the pediatric department, and the diagnosis of encopresis was not made if the child was under two years of age or if any physical finding could be logically considered to be the direct cause of the soiling.

ENCOPRESIS IN THE MENTALLY RETARDED CHILDREN

Twenty-six of the 70 encopretic children were feebleminded. Twenty-one had intelligence quotients below 50 (idiots and imbeciles) and 5 had I.Q.'s between 50 and 70 (morons). Approximately 4.8 per cent of all the feebleminded children, about 14 per cent of the idiots and imbeciles, and about 1.3 per cent of the morons seen in the clinic were encopretic. Their ages varied from two years, three months to ten years. In 16, however, the mental age was less than two years; in the other 10 it ranged from two years to five years. Twenty-one were boys, 7 were colored, and all but 4 were enuretic.

Ten of the 70 encopretic children were of borderline intelligence (I.Q. 70 to 80). This is about 2.6 per cent of the children of this intellectual level seen in this clinic. Nine were boys, 5 were colored, and all were enuretic. Their ages ranged from three to eleven years.

There was one child in the group whose I.Q. was not determined. This was a six-year-old colored girl with a history of masturbation, enuresis, and encopresis, who at the time she was seen at the clinic had a toxic delirium following a skin graft for a large burn. She later received her first adequate training from the nurses on the ward, resented it, and reacted to it with a good deal of trickery.

ENCOPRESIS IN THE CHILDREN WHOSE I.Q. WAS 80 OR ABOVE

Thirty-three of the 70 encopretic children had I.Q.'s of 80 or above. This was about 2.2 per cent of all the children seen in the clinic with dull normal, normal, or superior intelligence. The I.Q.'s were as follows:

I.Q.	NUMBER OF CHILDREN	I.Q.	NUMBER OF CHILDREN
80-85	4	105-110	2
85-90	4	110-115	1
90-95	7	115-120	0
95-100	8	120-125	0
100-105	5	125-130	2

Twenty-nine were male; 4 were female. Thirty-one were white; 2 were colored. Their ages were:

AGE	NUMBER OF CHILDREN	AGE	NUMBER OF CHILDREN
2 years 5 months	1	8 years	5
2 years 9 months	2	9 years	4
3 years	1	10 years	1
4 years	2	11 years	1
5 years	2	12 years	0
6 years	7	13 years	0
7 years	6	14 years	1

THE COMPLAINT

It should be emphasized that in most of these patients encopresis was one of a number of complaints. It was the only complaint in 3 of the 33 intellectually adequate children. It was the chief reason for reference in 3 others. In 17 it was one of several complaints (6 or less) and in 10 it was one of many (more than 6). One accusing mother glibly elaborated on 16 complaints. Associated complaints which occurred more than once were as follows:

ASSOCIATED COMPLAINTS	NUMBER OF CHILDREN
Enuresis	20
Temper tantrums	11
Feeding difficulties	10
Poor school work	10
Fighting	7
Stealing	6
Disobedience	6
Nervousness	5
Stubbornness	5
Constipation	4
Misconduct in school	4
Lying	4
Fears (one each of father, storms, dogs, autos)	4
Running away from home	4
Pains	4
Crying easily	4
Restless sleep	4
Nailbiting	3
Destructiveness	3
Fear of dark	3
Fingersucking	3
Masturbation	2
Stuttering	2

Indistinct speech	2
Cough	2
Restlessness	2
Vomiting	2

Additional complaints which occurred once were: "fellatio, head-shaking, head-banging, night terrors, sleepwalking, hollers out in sleep, cruel, high-strung, talks to self, fidgety, inattentive, can't sit still, grouchy, cranky, excitable, negativistic, doesn't answer when spoken to, talks you dumb, setting a fire upstairs, truancy from school, doesn't want to use the toilet, left-handed, teases younger brother, picks on sister, can't talk (deaf mute), doesn't seem to hear (deaf mute)."

The length of time in which the encopresis had been present when the children were first seen in the clinic varied greatly. In 7 cases it had persisted from infancy; in 2 of these to the age of eight years. It had been present a year or more in 6 (the longest duration being six years) and less than a year (one to ten months) in 9. In one case it was said to have been present "a long time," in another "for some time," and in 9 the duration was not recorded.

There was a great variation also in the frequency of the soiling episodes:

FREQUENCY	NUMBER OF CHILDREN
Occasional	8
Daily	4
2 or 3 times a week	3
2 or 3 times a month	2
7 times a day	1
2 or 3 times a day	1
Every day at times	1
Once a week	1
Twice a week	1
4 or 5 times a week	1
Once a month	1
5 times in 7 months	1
3 times in 1 month	1
Irregular (2 or 3 times a day for about 2 days a month)	1
3 times	1
Not stated	4

The encopresis began in 2 cases when the child started to school, in 1 when the child was kept by the Salvation Army when the mother was ill, and in 1 it followed acute diarrhea. In 2 cases it occurred only at school, in 1 after scoldings, in 4 when the children were outdoors playing, in 1 at night in bed, and in 1 it was associated with wetting the clothes.

The parents' complaint was recorded as nearly as possible verbatim. This, in many cases, gives considerable insight as to the parents' attitude not only towards the problem but towards the child himself. Several typical complaints in regard to the encopresis were as follows:

Mother (of a three-and-one-half-year-old colored boy of average intelligence): "He would hide to have a movement in his pants and would get constipated if I tried to make him sit on the pot. I did this the same time each day but it did not work. Each time he would promise next time to ask for the pot, but would always hide under the table or behind the door, and then tell me about it after it was over. I would spank him and put him to bed for it. These would just make him nervous and jumpy, and he would stop having a bowel movement for a day or two and become constipated even though I would sit him on the potty for one and one-half hours and give him books to read and toys to play with."

Mother (of a nine-year-old white boy, I.Q. 89): "He used to soil his clothes until he was six years old. He said he was afraid to sit on the toilet. He was afraid he'd go down in the ground."

Mother (of a six-year-old white boy, I.Q. 83): "He has soiled himself 2 or 3 times a week the past year. For three months he has messed himself with feces when in the toilet alone. Recently he smeared feces on his shoes and hands. When I saw him he said, 'Smell, mamma, smell.' "

Boarding home mother (of a seven-year-old white boy, I. Q. 97): "He has soiled himself three times since I've had him when he didn't go to the toilet in time. The second time I didn't have any clean clothes and I put a diaper on him to shame him. That day at school he had plenty of time and I paddled him when he got home."

Mother (of an eight-year-old white boy, I.Q. 92): "About twice a week when playing, he comes home with his clothes soiled. He claims that he does not know it, but I think that is because he does not want to lose his playmates. He's too lazy to come inside."

Mother (of an eight-year-old white boy, I.Q. 90): "Then he had the bad habit of doing something in his clothes and I whipped him and rubbed his nose in it and made him wash them, and the next day he'd do it again."

Mother (of a six-year-old white boy, I.Q. 94): "The first time he had a bowel movement in his clothes was about a month ago. When I was undressing him to go to bed, I noticed a terrible odor in his pants. I said, 'What's the matter, are you too tired to wipe yourself clean?' Then I saw what he had done. I've spanked him for it several times. I've told him if he didn't quit it I'd rub it in his face, just to scare him, see. I've put him on the commode and he says, 'I don't have to,' and I say, 'You've got to sit there until you do,' and he cries and carries on. Then later I smell him and I spank him and tell him he is too big a boy for that. What are you going to do? He never did that when he was younger."

Mother (of a fourteen-year-old white girl, I.Q. 97): "The specific difficulty is that she is unable to control her bowels at various intervals. Just when these times appear I cannot say specifically because I feel she is afraid of telling me or permitting me to know. However, at different times I have found her soiled underwear hidden in various parts of the room, and when I have asked her about the reason or the cause, she remained silent and sullen and passed it off nonchalantly."

ETIOLOGIC FACTORS WITH ILLUSTRATIVE CASES

From investigation of the causes of the encopresis in the 33 children with adequate intelligence, it becomes evident that the condition, in most cases, cannot be considered to be due to any one specific factor. There is usually a combination of such factors as make-up, unhappy home environment, interpersonal conflicts, lack of training, social difficulties, school difficulties, and fears. A clean-cut classification as to etiology is therefore not possible. Each case must be considered individually, and even then, from the information available, a clear explanation of the difficulty is not always obvious.

Outstanding, however, is the fact that many of these children came from unhappy homes. At least 12 of the homes could be considered to be highly undesirable environments for the rearing of children. In 4 cases the parents were separated. Four fathers were alcoholic; 1 was epileptic. Three fathers and 6 mothers were mentally deficient. One mother was an irresponsible vagrant and prostitute. Two fathers and 1 mother were paranoid. Such homes, obviously, were characterized by emotional tension, personal friction, and lack of effective training.

An example of such a home was that of F. K., a healthy six-year-old white boy of dull normal intelligence, who was referred because of stealing, lying, running away from home, bad temper, cruelty to animals and children, destructiveness, and encopresis of one year's duration. The child was reared in an atmosphere of tension and discord and never had any sympathetic or consistent training. The father, alcoholic and lazy, frequently accused the mother of infidelity and on one occasion chased her with a butcher knife. The mother, who divorced her first husband, was feebleminded, hypochondriacal, and once attempted suicide. After several temporary separations, the parents decided to separate permanently; the mother went to work, and the patient was placed in an orphanage at the age of four years. There his conduct became so bad that the orphanage refused to keep him. His behavior gradually became more serious. He ran away, shut himself up in a gas oven and was dazed when found, jumped from box cars, turned on gas, set fire to his mother's bed, fried dog's dung and ate it with mustard, carelessly fell out of a second story window, sustaining a skull fracture; at school he ate crayons, tried to choke a girl, and drank out of the toilet bowl. Institutionalization was recommended but it was eighteen months before he was placed in the State Training School for Feebleminded. Two years later, because he was not feebleminded, he was transferred to a boy's training school where, about two months later, the only complaints made about him were that he was inattentive, restless, and tore his clothes, supposedly unintentionally. His encopresis persisted fourteen months after he was first seen in the clinic.

Occasionally one finds a home in which there is actual parental hostility towards the child. C. A., a seven-year-old white boy of average intelligence, whose physical examination revealed hypertrophied and chronically infected tonsils, dental caries, eczema behind the ear, and vasomotor instability, was brought by his stepmother who accused him of fellatio, lying, stealing, enuresis, and encopresis two or three times a week. His parents separated when he was two years old. The father said that the mother ran around with other men and deserted him. The mother said that the father drank excessively, went with a

fifteen-year-old girl and other women, and that when she left him she took the child with her. She later obtained a divorce and the court gave the child to the father because she had no means of support. The boy then, for a period of three years, lived with relatives who had no complaints to make concerning his behavior. Two years before the child was seen in the clinic, the father remarried and the patient went to live with his father and stepmother. As investigation of the home proceeded, it became increasingly evident that the stepmother, and probably the father, wanted to get rid of the child. The stepmother exaggerated the boy's misconduct in order to convince the neighbors that he was a terrible child and that she was justified in her attempt to have him placed in an institution. Social workers, feeling that the home was not a good one, tried to place him in a boarding home, but the father, when he discovered that he would have to contribute to the boy's support, suddenly became very fond of the child and told the stepmother if the boy were taken from the home, he would leave. The stepmother, not relishing the thought of losing a source of support, also expressed her fondness for the boy. The domestic difficulties were thrashed out in court and a better understanding was brought about. Six months later the child's encopresis had ceased and the stepmother defended him as ardently as she formerly had accused him. His teacher reported that his school conduct was much better.

In one case unhappiness in a boarding home was the essential etiologic factor. J. H., a white boy, seven years, ten months old, of average intelligence, physically healthy, and of good parentage, was referred because of misconduct and lack of application at school, frequent soiling of his clothes, lying, stealing, and fighting. The encopresis began while he was at summer camp. He was sly about it, hid soiled garments, but was detected and punished by being made to wash his clothes. This child was a well-behaved boy until two years before he was first seen in the clinic, when he was placed in a boarding home because it was suspected that his brother had tuberculosis and his parents did not want him to be exposed. The boarding mother, a former school teacher, was strict with him and left much of his care to her 3 daughters, the youngest of whom (ten years old) the patient did not like. The situation became such that he was in constant disgrace and very unhappy. He was therefore returned to his home. The encopresis stopped promptly, his conduct and school marks rapidly improved, and four years later he was found to be a well-adjusted boy.

In 7 cases an important etiologic factor was an oversolicitous, overprotective attitude on the part of the mother. Not only were these children spoiled, inadequately trained, and not allowed to grow up emotionally, but some were made miserable by a strange mixture of indulgence, anxious hovering and nagging.

An example of the effect of spoiling was M. B., a healthy four-and-one-half-year-old boy of superior intelligence (I.Q. 126), who was brought to the clinic by his mother at the suggestion of his nursery teacher because he was nervous and had soiled his clothes five times in school. The child's mother separated from the father because he was alcoholic and failed to support her. The mother had only a fourth grade education, was emotionally childish, and was overindulgent towards the patient. At home there was played a "family game": the mother was supposed to be the father, the eight-year-old sister the mother, and the patient the baby. The mother and sister had the habit of carrying the child around like a baby, and in their presence he was very babyish. A more sensible

home atmosphere resulted in immediate cessation of the encopresis, and four years later it was reported that the child was doing well in school and was well adjusted at home.

In addition to the spoiling, in 2 cases there was a home atmosphere permeated with preoccupation with body sensations, fear of disease, concern over heredity, and superstitious medical notions. C. E., a healthy four-year-old white boy, of average intelligence, was referred because he had a dry cough and "stiff knees" for which no organic cause could be found, was nervous, bit his nails, ate poorly, vomited, and slept poorly at times. There was a history of finger-sucking, earpulling, breathholding spells, temper tantrums, fear reactions, and occasional encopresis. The child had an anxious, oversolicitous mother who was upset by "every little thing." The father was thought to have a "gastric condition," was on a diet, and the mother feared that the child had inherited it. The spoiling of the child was helped along by an overindulgent grandmother and two fond maiden aunts who lived in the same house. It was advised that the father submit to a physical examination, that the mother give up her notions of heredity and her oversolicitious attitude, and that the domination by the child of a group of enslaved females come to an end. The mother later expressed her gratitude for her relief from worry about the boy's physical condition. The father, with the encouragement of a physician, gradually resumed taking a normal diet. For about three and one-half years the child continued to soil occasionally when he was outdoors playing. Four years after the first visit to the clinic the mother reported that he had not soiled for six months and, except for poor appetite and occasional temper outburst, was getting along well at home and at school.

In the case of J. W. the bowel trouble resulted from the mother's constant preoccupation with bowel activity and her prevention of normal bowel function by the daily use of enemas and cathartics, until the child rebelled at the mistreatment. This child was a white girl, five years, four months old, in good physical health and of superior intelligence (I.Q. 128), who was brought by her mother because of chronic constipation and refusal to go to the toilet. In addition to this she presented feeding difficulties, restless sleep, temper tantrums, enuresis, and occasional soiling. The maternal great-grandmother, maternal grandmother, and mother all had a history of chronic constipation, although the mother's constipation ceased when her interest was directed toward her daughter's bowels. This suggested to the mother that the child's constipation was inherited. She had, however, developed other theories to explain the constipation, the latest of which was an etiologic connection between the constipation and a malformation of one of her nipples which she felt should not have been used in nursing. Constipation had been the chief topic of conversation in the home for years, and it was said that the father was tired of it all and tired of the mother. The child had been given hundreds of enemas, innumerable purgatives and gallons of mineral oil, which she hated and fought. An attempt was made to dispel the mother's notions and to persuade her to give the child's bowels a chance to function normally. The girl was placed for a time in a summer camp, where her bowels moved normally from the start, and about a year later it was reported that she was getting along well.

Fear seems to have played an important part in the case of H. E., a white boy, six years, nine months old, of average intelligence, and physically healthy except for infected tonsils and carious teeth, who was referred because he was failing in school, had night terrors, walked in his sleep, wandered away from home, was afraid to go to the bathroom even in the daytime, and, since a car accident at the age of four years in which he was not seriously hurt, had been

afraid of cars, had wet his clothes frequently, and had soiled his clothes twice a week. He was found to have a reading disability and in the next few months was given reading training. His tonsils were removed and he received dental care. The father, an uneducated chronic alcoholic, who did not support his family adequately, was in the habit, during sprees, of telling the boy blood-curdling tales at bedtime. Social work with the family came to a standstill because of the father's indifference and laziness. As part of the psychiatric study, Dr. J. H. Conn,[11] in order to determine the child's attitude toward the soiling, and his imagination associated with it, placed the child in a play situation in which dolls were used. In a number of such sessions over a period of about eighteen months, the boy explained that he was afraid to go to the bathroom because he feared that spooks, bogy men, ghosts, and kidnappers might cut off his penis and otherwise hurt him. He also feared that a mouse might chew off his penis. Later he identified the ghosts with his father. As his fears were brought out into the open and discussed sensibly, he gradually lost them. His enuresis stopped, the soiling decreased in frequency from twice a week to once in three weeks, and at the last interview (May 22, 1937) he had not soiled for three weeks, was going to the bathroom regularly alone, and talked as if his fears were things of the past.

A jealousy situation played an important part in the behavior of D. D., a seven-year-old white boy (I.Q. 106), who was brought by his mother with the complaints that he banged his head when he awakened in the morning or if aroused at night, giggled at everything whether it was funny or not, was slow in performing tasks, soiled his clothes about 3 or 4 times a month the past two years, teased his little brother, and was a "cry-baby." His school teacher complained that he did not apply himself or finish his work, acted silly, and was annoying, dependent, and a "disorganizing force" in the classroom. The patient had been a well-behaved child until the age of two years when an older sister died. The mother, greatly upset by this, allowed the child to get the upper hand. The encopresis began after the birth of a brother. In the play situation the child explained that when he bumped his head he imagined that he was rocking himself to sleep like a baby. He wet and soiled his pants because he wanted to be like a baby. He hurt his little brother because his mother scolded him and did not scold his little brother. He wanted his mother not to scold him and he wanted to play with his mother like a baby. The child was also found to have a potential reading disability and was given reading training. The mother was advised to praise good behavior and to ignore, as much as possible, undesirable behavior. The boy was sent to a convalescent home where he was frequently mixed up in some teasing and pounding scrape. He sat around much of the time with his mouth open as if in a daze, and the children considered him "no good." The encopresis stopped after two months, and about a year later the mother reported that he was behaving better and doing better in school.

One eight-year-old girl who soiled her clothes irregularly said she did it because she did not like her mother and wanted to be bad. In explaining the motives of a doll who was assumed to be enuretic and encopretic she said, "She is trying not to do what her mother tells her to. She doesn't want to listen to her mother. She worries her mother when she makes number 1 in her pants." Another little girl doll was brought into the situation and was supposed to ask her why she didn't listen to her mother. She said, "I want to be sassy." (Why?) "I want to be bad 'cause I don't like my mother." (Why doesn't she like her mother?) "She hits her." (Does she think her mother loves her?) "No sir, her mother likes her father better than her." (What does she say?) "I'm going to be sassy. I am going to be mad with you. I am going to make number 1 in my

pants." This little girl (I.Q. 107) was the younger of two unwanted children of a superstitious, hypochondriacal mother of borderline intelligence, and a reticent, sensitive, immature father. After years of domestic friction and economic strain which brought the mother to a psychiatrist, the parents separated and the mother found some happiness in the attentions of a forty-one-year-old "boy friend" who was a widower with 5 children. As would be expected, there were other behavior disturbances. The child was enuretic, had a poor appetite, was irregular in her sleep habits, had complaints of pains here and there, and in the past had had night terrors. Except for chronically infected tonsils and dental caries she was physically healthy. She has been under treatment about three months and in this period has soiled on two occasions.

Eighteen of the 25 intellectually adequate children of school age presented school difficulties. Eleven were doing poorly in school work; of these 4 had failed at least once. Ten presented behavior problems in school. One child was expelled from school because his teacher "could do nothing with him." One little boy who started to school before he was mentally quite ready for it came home from school frequently with his clothes soiled; he had not soiled before.

It is interesting that 5 boys with encopresis had some degree of reading disability. The most striking case was that of R. S., an eight-year-old white boy of average intelligence (I.Q. 92) whose mother complained that he was very inattentive, didn't mind anything she said, was always squirming around, wouldn't eat, scratched his back "something terrible" at night, was afraid of the dark, was doing poorly in school; didn't like his teacher, and came home from school about twice a week with his clothes soiled. Physical examination revealed malnutrition, poor posture, evidence of old rickets, chronic upper respiratory infection, thick, scarred eardrums, mild conductive deafness, and scabies. In spite of all this the child said, "I feel pretty good but my mother thinks I'm sick. I make out I can't hear and she thinks I can't." In addition to pediatric care, the child was given special reading training. Two months later the mother exclaimed, "Doctor, there has been a great change in R— the last month and I don't know what causes it. He never soils himself." Six months later his teacher reported that although he still did not do well in reading, he was not such a problem in class.

In some cases, as has been mentioned, from the data available it was difficult to understand the causes of the encopresis, the motives behind it, and the purposes which it served, and such children sometimes did not respond well to treatment.

A. R., a normally intelligent, attractive, and sociable girl, who was nearly fifteen years old and who seemed physically healthy except for slight obesity and mild chronic sinusitis, began to soil her clothes at the age of twelve following a diarrhea which was variously diagnosed as diverticula of the rectum, spastic colitis, Hirschsprung's disease, amebic dysentery, and "nothing wrong organically." For three years she had discharged fecal matter both in the daytime and at night at home, at school, at camp, and in spite of supposedly regular bowel movements in the toilet twice a day. She was the older of two children of a hypochondriacal father and a "nervous, irritable," and domineering mother. She started out in life with feeding difficulties which persisted to her tenth year, slept poorly and had nightmares, was enuretic to the age of 10, and in early child-

hood had frequent bouts of diarrhea, frequent attacks of pyelitis, and repeated upper respiratory infections often complicated by otitis media. The mother was very considerate with her regarding the soiling. She never punished, called the occurrences accidents, praised and rewarded for clean periods, sent her to the country with a special nurse "for a change of environment," and, on one occasion, arranged a dramatic ritual of burning all her underwear in the incinerator and buying a complete new outfit of underclothing. It was remarkable that the girl discussed the matter without the slightest display of embarrassment. She stated that she did not think her accidents were beyond her control; if she made a little more effort she could easily overcome them. She accepted the offer of help as a "good idea," readily assented to returning for interviews, but gave no convincing expression of a need for help. During interviews the next three months she persisted in her superficial attitude and repeatedly said that she was much better, although her mother continued to find soiled garments hidden about the house. During this period she refused to submit to a rectal examination, and when she finally did a fecal impaction was found. X-ray and proctoscopic examinations revealed an enormously dilated rectum with no evidence of pathology in the sphincter area or in the rectum. Although the possibility of congenital megalorectum was considered, Dr. Thomas R. Brown expressed the opinion that presumably the whole picture was "due to increased accumulation with its associated progressive dilatation of the rectum, a behavioristic syndrome, possibly with bad intestinal habits over a long period of time in a very spoilt, difficult child."

Fifteen of the 33 intellectually adequate children were found to be physically healthy. Three were constipated. One had x-ray evidence of dilated rectum. In one, spina bifida was found by x-ray, but this was not associated with neurologic findings. Others had various physical findings which were not considered to be of direct etiologic significance in the encopresis.

TREATMENT

Treatment in these cases is not directed solely towards relieving a symptom, but is rather planned to help the child to make a better adjustment in whatever sphere there seems to be difficulty. In other words, the child, rather than the encopresis, is treated, and in many cases the course of the encopresis runs a close parallel to the improvement in the general adjustment of the child.

Each child, of course, should have a careful physical examination, and physical abnormalities should be corrected as far as possible. Even though such conditions as malnutrition, chronically infected tonsils, or constipation cannot be considered to be direct causes of the encopresis, they may contribute to the child's unhappiness and interfere with his ability to make adjustments.

If treatment is to be effective, it is essential that the physician have an understanding of the environmental situations to which the child is attempting to adjust. He needs information concerning the intellectual level, economic and moral standards, and emotional atmosphere of the home. Economic difficulties may require the aid of social agencies, mari-

tal maladjustment may need amelioration, physical illnesses or personality difficulties of the parents may require medical attention, and medical misinformation and superstition may need correction. Many of the parents need advice as to habit training. Bowel training may be neglected, carried out inconsistently, or interfered with by faulty disciplinary methods. Severe punishment, shaming, and humiliating seldom result in the desired effect, but rather tend to cause in some children feelings of guilt, anxiety, and loss of self-confidence; in others, resentment and spitefulness. Excessive leniency and overindulgence may encourage soiling to gain attention or to control the family. Lack of parental affection may result in encopresis as an attempt to win sympathy or as an expression of hostility. Parental favoritism may foster jealousy and result in soiling as an expression of resentment. When the home environment is seriously at fault and proves to be unmodifiable, placement of the child in a foster home or boarding school may offer the most hope of improvement. In many cases school adjustment needs consideration. Unhappiness often results when the child is placed beyond his intellectual capacity in school and pressure is brought to bear both at school and at home. Reading disability should be thought of in children with adequate intelligence who are failing in their work, and when this is found, it requires special reading training by one who is familiar with this type of handicap. Some of the children need help with their social adjustment. Adequate and supervised play, cultivation of friendships, and development of interests and hobbies may contribute to the child's happiness.

An important part of treatment is work with the child. A sympathetic and uncritical physician can often win the child's confidence so that the child will talk freely of his troubles, fears, and dissatisfactions. Occasionally, a child will be delighted to discover for the first time that he is not a victim of heredity or that he does not have some disease or weakness, or that he is not just bad or lazy. The physician may utilize the good feeling towards him to give the child understanding as to why he behaves as he does and to offer suggestions as to how he may solve his problems in ways personally more satisfying and socially more acceptable. The smaller child's cooperation in overcoming his soiling may often be obtained by having him keep a star chart and letting him work for a prize. Slight improvement should be generously praised, and the child thus learns that soiling is a habit which he can overcome if he really tries. When pride or fear prevents the child from discussing his soiling frankly, the use of play situations and the discussion of the soiling in the third person with the use of dolls sometimes serves the same purpose.

In many cases encopresis responds quite satisfactorily to such treatment. Five of the 33 intellectually adequate children stopped soiling

immediately after the first visit to the clinic or after the recommendations were carried out; in 12 the encopresis stopped within six months; in 2 it persisted for about a year. Children from homes which are difficulty to modify because of lack of cooperation or personality inadequacies sometimes continue to soil for longer periods, and occasionally a child will be found who taxes to the utmost one's therapeutic resources. Five of the 33 children continue to soil for about two years, one for three and one-half years, and one child whose parents failed to carry out recommendations and did not return for further help was still soiling his clothes once or twice a week after five years. Five of the 33 children have been seen recently and are still under treatment.

SUMMARY

Encopresis, or involuntary defecation not directly due to organic illness, occurred in 70 or 2.9 per cent of the 2,406 children referred to the Psychiatric Clinic of the Harriet Lane Home for Invalid Children from Nov. 1, 1930 to March 11, 1937. Twenty-six of these encopretic children were feebleminded, 10 were of borderline intelligence, and 33 had I.Q.'s of 80 or above. Fifty-nine were boys, 11 were girls. In most cases the encopresis was one of a number of complaints. Outstanding etiologic factors are illustrated with brief case reports and treatment is discussed.

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THE QUANTITATIVE COLLECTION OF URINE FROM SMALL CHILDREN

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IT BECOMES desirable at times to obtain complete twenty-four-hour urine specimens of babies or small children. In general, the metabolism frame is used and if it is possible to have several sizes in order to fit children of different ages it is a satisfactory method of collection.

In studies on the metabolism of vitamin C not only are quantitative urine collections essential but the urine must be kept cold, dark, and

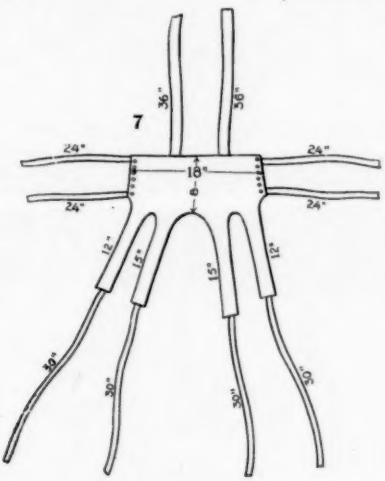

Fig. 1.

protected from atmospheric oxygen. This fact, in addition to the desire to follow babies from the first day of life, made it necessary for us to devise some other method. After many adjustments the method here illustrated was found to be highly satisfactory. It is offered as a suggestion of a simple inexpensive method which affords a minimum of discomfort to the small patient.

The first 4 pictures illustrate the type of apparatus used on small boys.

Figure 1 shows a restraining jacket which was found to be well adapted to the purpose. The measurements here given are for one of

From the Department of Pediatrics, The University of Rochester School of Medicine and Dentistry, and the Strong Memorial and Rochester Municipal Hospitals.

medium size—in all we have 5 different sizes with corresponding measurement adjustments. The material from which they are made is heavy, unbleached muslin of double thickness.

Figure 2 illustrates the position of the restraining jacket on the bed. The mattress is slightly elevated at the top to facilitate drainage but not enough to cause the child to slip toward the foot of the bed. A space

Fig. 2.

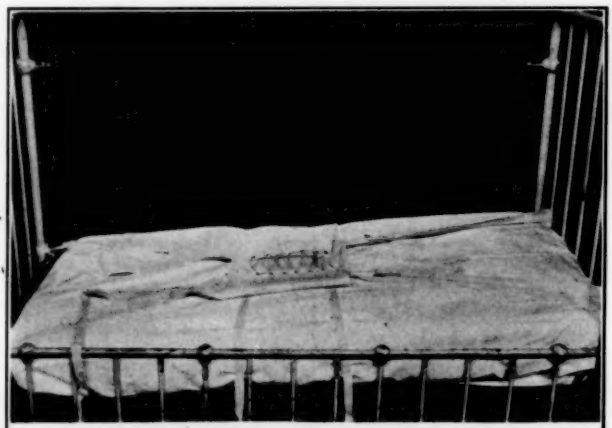

Fig. 3.

is left between the bottom of the mattress and the foot of the bed so that the collecting flask may be held in a slanting position.

Figure 3 shows the baby in position inside of the restraining jacket. The child is held firmly but at no point is restraint bothersome. At this time, before tying the bands of the restraining jacket which hold the legs (one in position and one still loose in this picture) the collection apparatus illustrated in Fig. 4 is adjusted.

Figure 4 is a sketch showing the details of the collection equipment. Into the middle of a double thickness piece of gauze 8 by 12 inches (*A*)

is inserted a piece of pyrex tubing 3 inches long (*B*). The diameter of the piece used is determined by the diameter of the penis of the child. The tube must fit well up into position but not too tightly. The under side of the tube is concave and rounds smoothly to a convex upper side. This makes close adjustment possible with maximum comfort. The tube is held into position in the gauze by a narrow piece of adhesive which may be seen in the sketch. The corners of the gauze are drawn around the legs and pinned to the band or skirt of the child. This gauze square (*A*) holds the tube (*B*) firmly and obviates the need of adhesive tape against the tender skin of the child except in minimum amounts. Six strips of adhesive tape are used. The first 2 tapes are placed on either

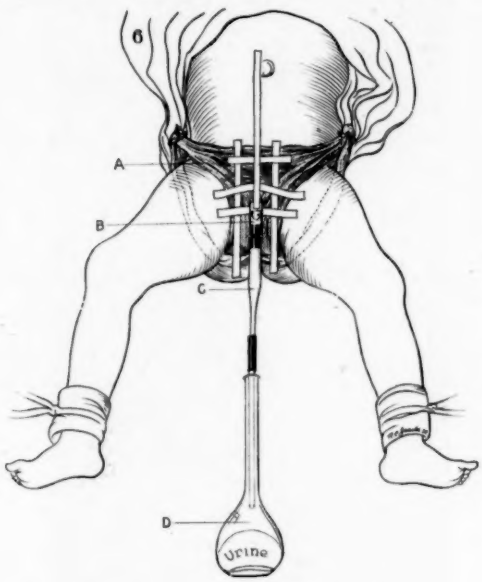

Fig. 4.

side in the groins in such a way as to hold the gauze firmly in place, the third is placed as close up under the tube as the gauze permits. The fourth piece holds the tube from above. The fifth tape is used only as a precaution against the first two being loosened by activity of the child. The last—the long piece—holds the top of the tube in the correct position. This tape should be long enough to make firm contact with the child's body. A tapering piece of pyrex tube (*C*) is then connected to the first piece (*B*) by means of a thin-walled tubing. This rubber serves as a flexible joint and prevents the tube (*B*) from being pushed too tightly against the child as might happen if the child was especially active. A second rubber connection is inserted before the glass tubing

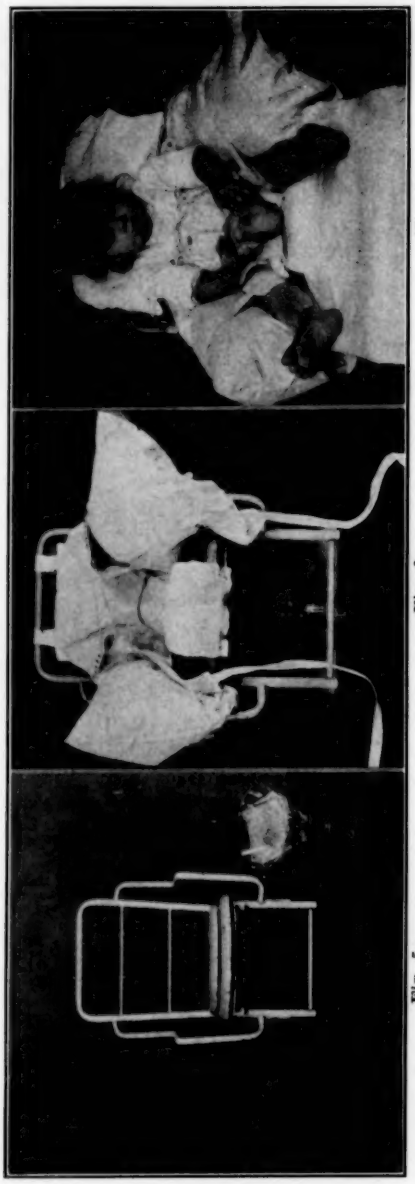

Fig. 7.

Fig. 6.

Fig. 5.

which goes into the neck of the 250 c.c. volumetric flask (*D*) which serves as a collecting bottle. The glass tubing should be sufficiently smaller than the neck of the flask to permit free movement.

For purposes of vitamin C study, the flask may contain glacial acetic acid, be immersed in a dish of cracked ice and be covered with a black cloth as means of preservation of the vitamin during the collection period.

The flask is easily disconnected and emptied for period collections by disconnecting at the lower rubber junction. The stool can be readily caught on a diaper or on a piece of glazed paper.

Figures 5, 6, and 7 illustrate the method of quantitative collection on small girls any time after they are large enough to be tied onto the nursery chair. We have as yet been unsuccessful in obtaining quantitative specimens on very small baby girls. The chair seat is padded by an inflated rubber ring which is covered and held in place by pieces of cloth (diapers). These protect the baby from contact with the rubber.

A gauze of monel metal in the short stemmed glass funnel catches the stool but permits the urine to run directly into the collecting bottle.

As pictured, pillows pad the chair arms and back and are held in position by the restraining jacket. The child, when laced into the jacket with her feet resting on a padded box, can very comfortably sit on such a chair for a twenty-four-hour collection. The restraining jacket permits enough adjustment without loss of urine to enable the child to obtain satisfactory rest and sleep. By adjusting the size of the restraining jacket and the size and number of the pillows the same chair may be used for children from six months to three years of age.

Critical Review

CONGENITAL SYPHILIS

Part I. Incidence, Transmission, and Diagnosis*

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THIS review includes summaries of the more important contributions to the knowledge of congenital syphilis that have appeared in the literature since the publication of the last discussion of the subject in this journal.[53]

DEFINITION OF TERM

The term "congenital" syphilis has been used in this report to designate syphilis contracted by an infant before birth. The terms "congenital," "prenatal," and "hereditary" are in more or less common use, but none of them is altogether satisfactory. The terms "congenital" and "hereditary" are found in the literature as early as 1839, but there does not seem to have been any clear distinction between them until much later. The term "prenatal" was used by Kolmer[32] as early as 1920.

"Congenital" (*congenitus*—born together) syphilis as used in this report is syphilis present in the infant at birth and acquired from the mother either by transmission through the placenta while in utero or during passage through the birth canal during labor. The disease is, therefore, always present at birth, although it may not become manifest until later. There are two objections to the use of the term "congenital." The first is that it does not indicate that the disease was acquired *from the mother*, who must necessarily be infected. Other forms of congenital defects, such as anomalies of the heart, are acquired in utero, but they are not necessarily present in the mother. The second objection, which was raised by both Stokes[55] and Rietschel,[50] is that the term implies an infection acquired at birth, not merely one present at birth. (This, however, is not the common use of the word as applied to other types of congenital defect.) Stokes[55] considers that "congenital syphilis" in the sense of infection acquired during labor is rare, and that it represents an infection resembling more closely the acquired infection of adults than the overwhelming tissue invasion and toxemia produced by transplacental infection.

"Prenatal" (*prae* + *natalis*—before birth) is a term introduced by Kolmer to indicate that the infection was acquired during intrauterine life rather than during labor. Thus it answers one objection to the term congenital, but it gives no information as to the source of the infection. Stokes[55] has accepted this term.

"Hereditary," although often used in the literature interchangeably with "congenital" or "prenatal," is a misleading term because it

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*Part II (to be published) contains the review of the literature dealing with prevention and treatment of congenital syphilis.

implies an infection present in either egg or sperm. True hereditary transmission of syphilis may be possible, but definite proof that it occurs is still lacking. Jeans and Cooke[27] use the terms "hereditary" and "congenital" interchangeably. They argue that the disease is inherited in the same sense that property is inherited from a parent and that the terms do not necessarily imply participation of the germ plasm. This seems an unnecessary confusion of medical and legal terms.

INCIDENCE

In order to estimate the incidence of congenital syphilis in children at the present time and the potential danger that syphilis may be to future generations, it is desirable to know the number of cases of the disease in the total population. Since the reporting of cases of syphilis is incomplete, statistics on the incidence of the disease in both adults and children are incomplete and more or less fragmentary.

In 1923 the American Social Hygiene Association[45] reported the results of a survey, based on a questionnaire, which showed that 8.3 per cent of ante-partum patients (both white and negro) in fifteen clinics were syphilitic. In 1935 the association[15] conducted a similar survey in 74 ante-partum clinics and found that among 62,516 white women syphilis was present in 6 per cent and that among 1,708 negro women it was present in 18 per cent. Among the private patients of eighty-two obstetricians the incidence of syphilis ranged from 0 to 3.5 per cent.

In the same year (1935) the association cooperated in a one-day census of syphilitics which the United States Public Health Service was conducting in forty-nine representative communities of the United States.[60] From this census it was estimated that there are 518,000 new cases of syphilis every year, of which 31 per cent (162,000) are in women. Since many of these women do not receive adequate treatment, the number of cases of the disease in an active form accumulates from year to year and at any one time there are approximately 186,000 women in the country suffering from active syphilis. Considering all the cases of the disease both active and latent, it was estimated that approximately one million of the women of the country have or have had syphilis and have had insufficient treatment to prevent the possibility of transmission of the infection to the child.

According to the 1930 census there are 32,612,792 women in the age group 15 to 49 years, inclusive, and, if one million are syphilitic, then 3 per cent of all women of child-bearing age harbor the infection.

It is interesting to compare this incidence of syphilis of 3 per cent in all women with the 6 per cent incidence found at approximately the same time by the questionnaire survey of white patients in ante-partum clinics. The ante-partum patients represent a selected group in that their exposure to syphilis is probably greater than that of other women.

The problem of syphilis among pregnant women is increased when the effect of the infection upon the outcome of pregnancy is considered. In almost half the cases of women with untreated syphilis, pregnancy terminates in the death of the fetus or infant.[33, 39, 40, 62] When the infection in the untreated mother is recent and active, the effects of the disease on the fetus are more unfavorable than when the infection is latent. The Cooperative Clinical Group[8] found in a study of 431 patients that only 57 per cent of the infants born of syphilitic women

with positive Wassermann reactions escaped the infection, as compared with 81 per cent of infants born of syphilitic mothers with negative Wassermann reactions.

Fetal deaths caused by syphilis occur in the latter half of pregnancy, rarely before the fifth month. Syphilis is not a cause of early abortion, according to most observers.[10, 1] McCord,[39] however, considers that syphilis may be a more frequent cause of early fetal death than is now believed.

Syphilis not only produces the death of the infant in utero or of the newborn child, but it produces late manifestations of the disease in over half of those children who survive infancy.[63, 40] It seems probable that more than 80 per cent of the pregnancies in untreated syphilitic women end disastrously for the infant.

In spite of these facts it is generally agreed that syphilis does not constitute reason for performing an abortion since the results of adequate treatment during pregnancy are so satisfactory.[43] However, Moore thinks that sterilization is socially desirable for those prolific women who are most uncooperative concerning the treatment and who have already produced several syphilitic children.

The incidence of congenital syphilis in children is even more difficult to determine than that in adults. Because of a general lack of morbidity statistics concerning the disease, data for the whole country are not obtainable, and surveys of isolated groups vary markedly depending upon the composition of the groups studied. Because of the high mortality from congenital syphilis, the incidence of the disease is greater the younger the group studied. The incidence of the disease is higher among negro than among white children and varies inversely with the economic level.[59] From a compilation of reports in the literature made by the United States Public Health Service[58] the incidence of congenital syphilis among all children has been estimated as 2 per cent; when these data were restricted to infants only, the rate was 5.6 per cent. Among white children the rate is estimated to be 1.7 per cent, but among negro children, 12.2 per cent. When the data were considered in relation to economic status, it was found that the incidence of congenital syphilis among white children in clinics was 5.3, whereas among children of the well-to-do it was less than 1 per cent. From the one-day census the Public Health Service[59] estimated that of the 683,000 individuals with syphilis constantly under observation and treatment in the United States, at least 60,000 were suffering from an infection transmitted from the parents.

TRANSMISSION

For many years the literature has contained discussions of the means by which syphilis is transmitted from parents to children. At the present time the consensus of opinion in this country is that the usual means of transmission from a syphilitic mother to the fetus is through the placenta, even though the mother may show no detectable manifestation of the disease. Infection of the fetus probably does not take place before the fifth month of intrauterine life, since penetration of the placenta by spirochetes before this time has not been demonstrated. It is possible, however, for fetal infection to take place at any time between the fourth and ninth months.[35, 34, 19] The earlier the placental barrier is broken down, the more extensive will be the resulting invasion of the fetal tissues and the greater will be the chance that the

result for the fetus will be fatal either before term or soon thereafter. Fetal infection late in pregnancy may account for the birth of the apparently healthy infants of untreated syphilitic mothers, many of whom are reported to develop the disease months or years after birth.

The old law of Kassowitz[28] that the virus of syphilis becomes attenuated with time and that the infection slowly wears itself out is gradually being discredited as more and more reports are published in which the disease is shown to be considerably active many years after the initial infection. Jeans and Cooke,[27] reporting the fate of 3,009 children of 870 syphilitic families, show a remarkable constancy in fetal deaths and in deaths during early infancy, regardless of the duration of the syphilitic infection in the mother. Ingraham[22] studied the relation of the duration of the disease in the mother to the infection in the offspring and concluded that the difference in the incidence of syphilis in the offspring of syphilitic women is so little influenced by the duration of the disease in the mother that no reliance can be placed upon this criterion for prognosis.

Paternal transmission of syphilis is the subject of much discussion.[63] The theoretical explanation of paternal transmission rests upon the demonstration of a life-cycle variant of the spirochete small enough to adhere to the head of the spermatazoon. No conclusive demonstration of this has as yet been made.

The question of the transmission of syphilis to the next generation by those who themselves acquired the disease in utero (third-generation syphilis) is still debatable and will possibly always remain so. It is essential to prove that the mother of a congenitally syphilitic child received her own infection congenitally and that she did not acquire syphilis at any time during her life.[7, 44] Many reports have appeared in the literature to indicate beyond reasonable doubt that third-generation syphilis does occur, although it is probably not a common method of transmitting the disease.[7, 44, 52, 46] The routine treatment of congenitally syphilitic women during each pregnancy is advocated by Moore.[43]

DIAGNOSIS OF CONGENITAL SYPHILIS IN THE NEONATAL PERIOD

In view of the fact that it is desirable to treat a syphilitic infant as soon as possible after birth, the problem of making a diagnosis in the early weeks of life is important but sometimes difficult.[22] It is possible for an infant at birth to harbor the *Spirocheta pallida* in his tissues but to show no outward evidence of the disease.[49] This occasionally occurs in the infants of untreated syphilitic women, but it occurs with considerable frequency in the infants of partially treated syphilitic women.[22]

There are several procedures in common use for establishing the diagnosis in the fetus or living infant:

1. Demonstration of the disease in the parents.
2. Examination of the placenta and cord.
3. Examination of stillborn infant.
4. Clinical examination of living infant.
5. Serologic tests of the living infant.
6. Roentgenologic examination of the bones of the living infant.

Demonstration of the Disease in the Parents.—The first step in establishing the presence or absence of the disease in the newborn infant is that of establishing its presence or absence in the parents. It is

manifestly impossible for an infant to suffer from congenital syphilis if it can be proved that the disease is absent in both parents.

Examination of the Placenta and Cord.—The syphilitic placenta is larger than the normal. It is not its absolute weight that is signficant, however, but its increased weight in proportion to that of the fetus. Normally the placenta weighs one-sixth as much as the fetus, but in syphilis it may weigh one-fourth, one-third, or even one-half as much as the entire body weight of the fetus. Williams[64] believed that certain changes in the placenta were pathognomonic of syphilis and that these changes formed a basis for a diagnosis of congenital syphilis in 80 to 90 per cent of infants. Later reports have pointed out difficulties in making a positive diagnosis in the infant on the basis of histologic changes in the placenta.

Ingraham and Kahler,[25] for example, state that the demonstration of syphilis in the placenta indicates only a maternal infection and is not synonymous with infection of the infant. Jeans and Cooke,[27] on the other hand, state that in their opinion it is very doubtful if characteristic changes in the placenta can be found in the absence of syphilis in the infant. McCord in 1928[37] stated that a histologically syphilitic placenta means a syphilitic baby but that the converse is not true. McCord concluded in 1934[38] that the histologic examination of a syphilitic placenta, especially in a premature birth, is laden with so many difficulties that it is not of great practical value as a routine method of determining congenital syphilitic infection.

Examination of the umbilical vein has proved a valuable means of detecting syphilis. Philipp and Gornick[48] examined scrapings of the umbilical vein by dark field and found that they could frequently demonstrate spirochetes in the umbilical vein by this method even when the placenta was morphologically negative for syphilis. They found spirochetes in the umbilical vein wall in 5 of 15 dead syphilitic infants from mothers whose placental findings were negative and in 5 of 9 living infants who had negative blood Wassermann reactions. Klaften[30] used the same method and considers it a valuable procedure in making a diagnosis of early congenital syphilis.

Ingraham[23] also reported results of dark-field examinations of scrapings from the umbilical veins of 86 unselected infants of syphilitic mothers. Spirochetes were found in 24 fetuses (5 stillborn and 19 living infants). All but 2 of the 24 infants were ultimately proved to be syphilitic. The finding of spirochetes in the umbilical-vein examinations was the earliest diagnostic evidence of syphilis obtainable in 10 of the 24 infants. In 18 of the 86 cases in which the umbilical-vein scrapings were negative by dark-field examination, proof of syphilis was subsequently obtained by other means. Ingraham[23] concluded that the dark-field examination of the umbilical vein is a valuable diagnostic aid in the early detection of syphilis in the asymptomatic infant. When the result of the examination is positive, the infant has syphilis in almost 100 per cent of the cases, but when negative, syphilis in the infant is not, of course, excluded.

Examination of the Stillborn Infant.—Syphilis is one of the causes of intrauterine death, and, if the fetus is retained within the uterus, it undergoes rapid deterioration and presents the characteristic picture of maceration when finally expelled.[57] Maceration, however, is not

pathognomonic of syphilis. Stokes[55] states that "Strachan could only find 6 syphilitic fetuses among 24 macerated specimens, and Kehrer found syphilis the cause of maceration in 41.3 per cent of his cases. On the other hand, Tenconi found 80 per cent of macerated fetuses to be syphilitic, and Browne found 64 per cent in a careful study of 22 cases."

The pathologic picture presented by syphilis is one in which all of the tissues are involved. The most common type of early change is a diffuse inflammatory hyperplasia, and in general the amount of change is in relation to the function of the part during fetal growth.[11, 54] The spleen, liver, and bones suffer greater damage than other organs. The spleen becomes enlarged; the liver is retarded in development so that at birth there is frequently persistence of embryonic cells. Occasionally the kidney shows a similar arrest in development.[21, 27, 55] The pancreas shows a widespread fibrosis with a retardation in development. The characteristic syphilitic lesion in the lung is fibrosis with the production of irregular, firm elastic patches (pneumonia alba).[27] Adair[2] finds a tendency to a persistence of the nephrogenic zone in the kidney of the congenital syphilitic.

The most conclusive diagnosis of syphilis can, of course, be made by the actual demonstration of the *Spirocheta pallida* in the tissues. Adair[2] found spirochetes in the tissue in 41 of 46 syphilitic fetuses; Browne,[3] in 8 of 14 macerated fetuses but in only 1 of 21 nonmacerated syphilitic fetuses. Cruickshank's findings[10] were similar in that he found spirochetes in 7 of 9 macerated fetuses but in only 10 of 116 nonmacerated syphilitic fetuses.

The greater ease with which the organisms can be found in macerated fetuses may be due to the incubator effect of the uterus. Stokes[55] thinks that spirochetes may multiply rapidly in dead tissue under conditions simulating those in the uterus and suggests that these findings justify the incubation of organs of fetuses suspected of syphilis in the hope of demonstrating spirochetes. McCord,[36] however, finds it more difficult to demonstrate spirochetes either by dark-field examination or in stained sections when the fetus is macerated. Jeans and Cooke[27] report that spirochetes disintegrate after death and frequently disappear completely within a day or two after the death of the fetus.

Clinical Examination of the Living Infant.—Clinical signs of syphilis are obvious at birth in only a small percentage of syphilitic infants.[23] When signs and symptoms occur, the most common are snuffles, skin lesions, eye lesions, splenomegaly, lymphadenopathy, malnutrition, gastrointestinal disturbances, intracranial hemorrhage, and pseudoparalysis of Parrot.[23] While many of these signs are very suggestive of syphilis and should always arouse suspicion of the presence of the disease, they are not pathognomonic of syphilis and almost all are occasionally encountered in infants entirely free from syphilis.[21] Ingraham[23] listed the most characteristic signs of syphilis and recorded their incidence in the syphilitic and nonsyphilitic infants of 212 syphilitic mothers. He found that up to the age of 2 months definite obstruction to nasal breathing indicated syphilis in 88 per cent of the infants who showed this sign, splenomegaly in 71, bilateral epitrochlear lymphadenopathy in 51, marked scaling and fissuring of the skin at birth in 65, and syphilitic skin lesions and pseudoparalysis of Parrot in 100 per cent.

In view of the fact that many syphilitic infants show no clinical evidences of the disease in early infancy, Ingraham[23] concludes that from purely clinical studies the diagnosis of syphilis cannot be made with any degree of certainty in the first 2 months of life in as many as 5 per cent of the cases. If it is known[23, 12] that the mother is syphilitic, the presence of coryza, splenomegaly, unexplained malnutrition, or gastrointestinal disturbances, or continued fever of undetermined etiology should lead to the suspicion that the infant is syphilitic. A diagnosis of syphilis in the child must, however, be confirmed by other means.[51]

Roberts[51] found clinical signs of syphilis in 27 per cent of 237 syphilitic infants at birth. Syphilis could be diagnosed by clinical signs alone in 82 per cent by the age of 3 months.

Spirochetes have been demonstrated in various tissues and secretions of the living syphilitic infant. They are frequently found in the nasal and the conjunctival secretions, in skin lesions, in the blood stream, in the urine, and in the meconium.[20] Manteufel and Herzberg[42] have diagnosed congenital syphilis in obscure cases by inoculating either cubital or inguinal lymph gland emulsion into rabbits.

Serologic Diagnosis.—The value in the diagnosis of syphilis of serologic tests (Wassermann or Kahn) of the umbilical-cord blood or the venous blood of the newborn infant has been questioned. Fildes[17] first pointed out that antibodies present in the mother's blood might be transmitted through the placenta and appear transiently in both the cord blood and the blood of the infant in the absence of syphilis. In spite of many studies[13, 40, 18] which have substantiated Fildes' original view, the recent literature contains such statements as McCord's[39] that "in the vast majority of cases, a strongly positive cord Wassermann test, properly done, means that the baby has congenital syphilis," or Collardi's[9] that "the Wassermann reaction of the blood of the umbilical cord of the newborn has a distinct diagnostic value when positive, for it absolutely indicates fetal syphilis."

Ingraham[23] has tabulated, in a series of 195 infants, the various combinations of positive and negative cord-blood findings with the ultimate diagnosis in the infant with regard to syphilis. He found that the serologic reaction of the cord blood correctly predicted the condition of the infant in 64 per cent of the cases and failed to do so in 36 per cent. In those cases in which the cord blood was positive, 83 per cent of the infants developed syphilis, and 17 per cent remained free from all evidence of the disease. In those cases in which the cord blood was negative serologically, 60 per cent remained free from infection but 40 per cent developed syphilis.

On the basis of this study it appears that the statement that a positive Wassermann reaction of the cord blood is an absolute diagnostic sign of syphilis in the infant is not true for about 15 per cent of the cases, and the statement that a negative Wassermann reaction of the cord blood guarantees a nonsyphilitic infant is not true for about 40 per cent of the cases. Kilduffe[29] states that a positive cord-blood reaction is of value only as indicating further need for, and prolonged study of, the case.

Jeans[26] maintains that results of serologic examination of the infant's blood are of absolute diagnostic value after two months of life

have passed. Other observers have reported cases in which the blood has remained seronegative for six months or longer and has then become positive.[23] In nonsyphilitic infants the positive serology seldom persists for as long as two months and usually for a much shorter time. Twenty-two syphilitic infants reported by Ingraham to have positive blood Wassermann reactions at birth developed negative blood Wassermann reactions before leaving the hospital at 10 days of age.

Dunham[13] studied the Wassermann reaction of the mother's blood, the cord blood, and the blood of the infant in a series of seven cases in which there were no clinical evidences of syphilis in the infants at birth. All of the infants at birth had positive blood Wassermann reactions, but in all seven cases there was gradual weakening of the reaction until at the end of six months six of the infants had negative reactions. The seventh was not tested until the end of a year, at which time it had a negative reaction. The Wassermann reactions were repeated at intervals for a period varying between two months and four years, and the tests continued to be negative and no clinical evidences of syphilis developed in any of the infants.

Faber and Black[16] also studied a group of infants of syphilitic mothers, using a quantitative method for making the Wassermann test. They reported that nonsyphilitic infants with positive Wassermann reactions at birth show a gradual weakening of the reaction until it finally becomes negative, whereas the reactions of syphilitic infants usually show an increasing intensity during the same period. It was found that by the use of a quantitative technique a change in intensity of the Wassermann reaction was usually detectable during the first week of life, and it was suggested that such a change might prove a sufficient basis for diagnosis.

Christie,[5] using the quantitative Wassermann technique, confirmed the findings of Faber and Black. Tests of the cord blood of 14 infants of syphilitic mothers were positive in all but one case in which the specimen hemolyzed. Quantitative Wassermann tests of the blood repeated at intervals thereafter showed a gradual diminution in intensity until they ultimately became negative in 11 infants, none of whom showed any evidence of syphilis clinically or in roentgenograms of the long bones. Three of the 14 infants ultimately developed evidences of syphilis. In 2 of the 3 cases the intensity of the Wassermann reaction increased at each examination until other evidence of syphilis appeared. The third case was an exception since the blood showed a lessened reaction after the first examination, only to increase *after* the development of clinical signs of syphilis.

The work of Christie suggests that a comparison of the results of quantitative serologic examinations of the cord blood and the infant's blood may prove valuable in the differentiation of the pseudopositive but clinically well infant from the syphilitic infant at an earlier age than has heretofore been possible.

Roentgenologic Examination of the Bones.—Syphilis produces changes in developing bones which are usually recognizable roentgenographically. The roentgenographic method of diagnosis has been in use for thirty-five years. In spite of this long period of use, however, there still exist differences of opinion concerning the specific changes produced in the bone by the disease and those which represent the earliest manifestations of these changes in the roentgenogram.

In order to understand the changes in bone due to syphilis the underlying pathology must be appreciated. From pathologic studies[47] it has been shown clearly that congenital syphilis produces a fibrosis in developing bone which soon interferes with the blood supply, causing the formation of granulation tissue. Increased calcium deposition takes place within this granulation tissue without subsequent ossification. After granulation tissue has replaced normal vascular areas there may be actual pus formation with caseation and softening. Thus the syphilitic process in bone is characterized by both proliferation and destruction of tissue.[47]

In the roentgenogram this proliferation and destruction of tissue gives the appearance of areas of increased density and of rarefaction.[47] The pathologic changes seen in the roentgenogram are most marked in the areas of greatest bone growth, namely, the diaphyso-epiphyseal junctions and the periosteum, producing, respectively, osteochondritis and periostitis.[47] Osteochondritis is a very frequent lesion of early congenital syphilis. It has been found present at birth and during the later months of intrauterine life also. The incidence of the condition decreases as the age of the children examined increases. Periostitis, on the other hand, is a lesion which develops later, usually between the second and fifth months of life.[24]

Ingraham[24] concludes from his own studies: "We feel that we may assume with a reasonable degree of accuracy that syphilitic osteochondritis, other things being equal, becomes roentgenologically manifest about five weeks after the fetus is infected, while syphilitic periostitis requires approximately four months to develop." He believes that it is possible to approximate the time of infection of the child or fetus from the stage of the osseous lesions. According to Ingraham, most syphilitic fetuses are infected in the later months of pregnancy and are either born with lesions of osteochondritis or develop them within a short period after birth. Periostitis does not usually develop until the fourth to fifth month after infection. It is not impossible for a fetus to acquire syphilis early in pregnancy (any time after the fifth month), suffer from osteochondritis, and recover from it before birth. The roentgenogram at birth may appear normal but later may show evidence of periostitis as the first manifest lesion of the disease. Occasionally periostitis is found unassociated with other osseous lesions (5 per cent in McLean's[41] series). In such cases Ingraham feels that the osteochondritic process has healed rather than that it did not exist. It is, however, more usual to find periostitis accompanying other lesions, especially osteochondritis.

Epiphysitis is frequently present in the roentgenogram of syphilitic infants, according to Pendergrass and Bromer.[47]

Osteochondritis, periostitis, diaphysitis, and epiphysitis are the bone lesions commonly associated with syphilis in the newborn infant. Osteochondritis does not produce permanent deformity and, in fact, disappears spontaneously without treatment. Sutherland and Mitchell[56] suggest that it is a secondary lesion because of its ephemeral character. All the bone lesions of early congenital syphilis are widespread in their distribution. Practically all the bones, or very few, may be affected, although a single bone lesion is never due to syphilis.[41] The process is not necessarily uniform although multiple involvement is present.[47] Very mild involvement may be present in one bone while an extremely

severe process exists in another. Thus an examination of the entire skeleton is desirable before ruling out syphilis.[47] McLean[41] found that bone involvement is usually bilateral.

The syphilitic process is not the only pathologic one which alters developing bone tissue. A good deal of disagreement has arisen over the interpretation of certain transverse lines of increased density near the diaphyso-epiphyseal junction. Pendergrass and Bromer[47] have described transverse bands in syphilitic bone. Their explanation of the mechanism of formation of the band is that irregular interference with growth by the syphilitic process produces areas of calcification beyond the degenerate portion and forms transverse zones of provisional calcification at different levels.

Klaften and Priesel[31] consider transverse zones in bones to be evidence of successive attacks of osteochondritis and correlate them with the time of beginning syphilitic treatment in the mother. They report that the earlier the treatment begins, the further the bands have moved in the direction of the diaphysis; the later the treatment, the less the distance of the bands from the ends of the metaphysis. There are probably several mechanisms in addition to syphilis by which these lines are formed.

Caffey[4] has shown that bismuth administered to a woman during pregnancy passes through the placenta and is deposited in the long bones in transverse lines near the diaphyso-epiphyseal junction. He states that there is not enough bismuth deposited in the infant's bone to account entirely for the shadow cast in the roentgenogram. An increased calcium content, induced apparently by the presence of a small amount of bismuth, is responsible for this line, according to Caffey.

Before the advent of bismuth treatment for syphilis Eliot, Souther, and Park,[14] in making roentgenologic studies of children for rickets, observed transverse lines in the bones of these children. They concluded that these lines appear when for some reason the growth of cartilage is suddenly slowed or stopped and that, conversely, sudden increase in growth produces areas of rarefaction in the long bones.

It seems possible that this may be the basic physiologic explanation of all transverse lines. That is, some factor interferes with the normal growth of the bone and as a result the trabeculae develop laterally instead of vertically, causing an overlapping and lattice formation with an increase in primary bone formation. This interference with growth may be due to a nutritional factor, a drug such as bismuth, a poison such as lead, or an infective agent such as the *Spirocheta pallida*. If this is true, it makes the diagnosis of syphilis based on an interpretation of roentgenographic findings in the bones of newborn infants a difficult procedure.

Numerous reports dealing with the relation between the roentgenographic findings and other manifestations of syphilis have appeared. Many of them are difficult to interpret because full information in regard to findings is not always given. In 14 reports[61] made between 1921 and 1937 the incidence of bone lesions in cases of congenital syphilis varied from 23 per cent to 100 per cent. McLean,[41] for example, found bone lesions uniformly present in a roentgenographic study of 102 syphilitic infants and thought they were the earliest detectable manifestation of the disease.

Ingraham[24] states that the roentgenogram offers the most reliable means of diagnosis of syphilis in early infancy. He found that 29.1 per cent of the infants of his series showed characteristic roentgenologic changes during the first week of life, and that 78.8 per cent of the 90 syphilitic infants showed bone lesions in the roentgenogram during the first few months of life. Christie,[6] on the other hand, found the roentgenogram of help in diagnosing congenital syphilis in the neonatal period in only 2 of 83 cases.

It is difficult to come to any conclusions concerning the usefulness of the roentgenogram in the early diagnosis of congenital syphilis from a study of the published reports.

McLean[41] describes the following changes in the roentgenogram as pathognomonic of syphilis: (a) Well-defined saw-tooth metaphyses in well-calcified bones; (b) deep zones in the longitudinal axis of submetaphyseal rarefaction; (c) multiple separation of epiphyses with or without impaction in bones which are not rachitic; (d) bilateral symmetrical osteomyelitis of the proximal mesial aspects of tibia; (e) multiple areas of circumscribed osteomyelitis of long bones shown by the roentgen ray as patchy areas of rarefaction; (f) multiple longitudinal areas of rarefaction (osteomyelitis) in the shafts of the long bones, sometimes resulting in fractures; (g) destructive lesions at the mesial or lateral aspects of the metaphyses (foci of rarefaction); (h) multiple areas of cortical destruction generally seen within a centimeter of the ends of the bones; (i) double zone of rarefaction at ends of bones; (j) localized periosteal cloaking occurring in more than one bone.

These lesions are all those of advanced syphilis and are quite generally accepted as pathognomonic of syphilis. The controversy arises over the early signs of pathology and their differentiation from those produced by agents other than syphilis. The changes that are most likely to cause confusion in establishing the positive diagnosis of syphilis by the roentgenogram are (a) submetaphyseal rarefaction produced by very rapid growth;[14, 41] (b) transverse bands near the diaphyso-epiphyseal junction produced by nutritional disorders which temporarily slow up or stop bone growth;[14] (c) transverse bands formed by the administration of bismuth to the mother during pregnancy. Occasionally these bands are so dense that the bone immediately distal to them has by contrast a rarefied appearance;[4] (d) apparent thickening of the cortex of the bones of very rapidly growing premature infants. The more rapid calcification of the periosteum than of the shaft may be confused with syphilitic periostitis. It is usually more regularly distributed along the length of the bone framework than is the periostitis of congenital syphilis.[41, 6]

After a review of the available literature one is forced to conclude that the diagnosis of congenital syphilis in the newborn infant is often extremely difficult.

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SEVENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

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Round Table Discussion on Asthma and Hay Fever in Children

Chairman: Dr. Bret Ratner, New York, N. Y.
Assistants: Dr. William M. Schmidt, New York, N. Y.
Dr. Franklin A. Stevens, New York, N. Y.

Allergy as Related to Pediatrics

CHAIRMAN RATNER.—We are gathered here to discuss some phases of the problem of asthma in infancy and childhood. Only a few phases can be touched upon for lack of time. Dr. Schmidt will discuss hay fever; Dr. Stevens will take up the matter of infection in relation to asthma; I shall discuss some of the phases of allergy confronting the pediatrician.

While asthma has been regarded as a chronic disease affecting adults to the greatest extent, the experience of recent years has taught us that the disease often has its onset in early childhood; conditions that at one time were diagnosed as common colds and recurrent bronchitis, we now know may be the first evidences of hypersensitiveness. I am firmly convinced that it is to the advantage of the pediatrician to become acquainted intimately with the diagnostic and therapeutic phases of this subject because it is he who is called upon to treat this condition from its inception and is in the position to do the greatest good prophylactically. Approximately 50 per cent of allergy cases seen in children have their onset in the first year; by the fifth year, 80 per cent have already begun to present symptoms.

Does inheritance play a rôle?

A child does not inherit the same type of allergic syndrome from his antecedent, nor does he necessarily react to the same excitant. The allergic child inherits an ability to become sensitized, but such a capacity is not any more unique with an allergic individual than a normal one; it is a property common to the entire animal kingdom. The interesting thing is that irrespective of the attitude held on inheritance as a factor, all are agreed that adequate exposure to an antigenic substance is necessary before symptoms occur. In view of the uncertain state of our knowledge it seems to me that the attempt of some workers to establish a correlation with the Mendelian principles of inheritance has only tended to add to our confusion. My chief quarrel with the proponents of the inheritance theory is that, in the face of the absence of proof, to assume that an individual is predestined to develop hypersensitiveness forces a defeatist attitude upon us.

If, on the other hand, the postulate that asthma is an acquired condition is wholeheartedly accepted, greater efforts will be made towards its prevention. I believe that this has been the direction of the work of recent years. The following facts gleaned

from experimental data may serve as a basis for a consideration of preventive measures in the human being:

1. A state of hypersensitiveness may be acquired congenitally, that is, in utero.
tract under certain conditions.
2. Undigested food proteins can pass through the wall of the gastrointestinal
3. Inhalation of dry antigenic dusts can result in sensitization.
4. Subjecting native proteins to heat reduces their anaphylactogenicity.
5. Repeated infections may result in sensitization to bacterial proteins.
6. Drugs or chemicals entering the body may produce haptens and result in so-called drug idiosyncrasies.

We have demonstrated that the excessive indulgence in large amounts of protein foods by the pregnant female, particularly in the latter months of gestation, may establish a sensitization to these foods in the unborn child. About 30 per cent of our allergic infants suggested such an antepartum influence. The pediatrician must remember that antenatal or congenital hypersensitiveness may be accountable for reactions occurring upon first contacts with foods.

The vlulnerable period for the establishment of postnatal hypersensitiveness is the first two years of life when membranes are especially permeable, new foods are being introduced, and the child is exposed to new environmental contacts.

Similarly, during convalescence from a disease of any nature, the membranes are particularly permeable.

While 75 per cent of allergic children suffer from food allergy, only 15 per cent are sensitive to foods alone, whereas the remainder have a combination of food and epidermal or pollen sensitivities. This is important because there seems to be a misconception that infants and young children are almost entirely sensitive to foods. Bearing this in mind, the pediatrician must direct his attention towards the control of the child's diet and environment in order to reduce and minimize the incidence of allergy.

New foods should be partially denatured. They should be started in small quantities and gradually increased. While variety is necessary in order to avoid excessive amounts of any one particular protein food, the introduction of new foods should be gradual.

As for the environment, it should be kept simple and as free from dust-producing articles as possible. The child's wardrobe and toys are also possible sources of danger.

Drug sensitivities may develop when they are used excessively; prominent among these are aspirin, quinine, iodine, mustard, flaxseed, ipecac, bromides, phenolphthalein, mercury, and, might I add, sulfanilamide.

Serum sensitivity is in large measure due to a spontaneous sensitivity to horse dandruff or rabbit hair. There is every evidence to believe that parenteral injections of antisera given repeatedly may eventuate in serum sensitivity. Every precaution should be taken to prevent anaphylactic shock or death. One must ever be on his guard against such a catastrophe.

The pediatrician is therefore confronted with a multitude of preventive measures that he may institute in an attempt to diminish the incidence of allergy in childhood.

The diagnostic procedures are thoroughly covered in texts on this subject, and I will therefore not discuss them here.

Having established the etiologic cause of the asthma, there are two courses open with respect to treatment, (1) the elimination of the offending substances, and (2) desensitization. All agree that elimination is essential. But will elimination alone produce a good result, or is it preferable to build up an immunologic tolerance? That depends upon the nature of the offending substance; if it is one that the patient can easily avoid coming in contact with, elimination alone may answer the problem. If, however, it is a common factor in most environments, contact with which is

difficult to avoid, it is best to build up a tolerance. This is more particularly true of common foods; fortunately too, desensitization to foods can be accomplished with little danger to the patient by oral administration of minute amounts, instead of by injection. Dr. Schmidt and Dr. Stevens will take up the matter of desensitization to pollens and bacteria.

Specific knowledge will have to be acquired with relation to the exact form in which offending foods may be given without causing reactions. For example, we now know:

1. In the milk-sensitive patient, evaporated milk can be used, whereas pasteurized milk, buttermilk, and dry milks cannot.

2. Dextrimaltose can be tolerated by the patient sensitive to the barley and wheat, whereas malt extracts cannot. Corn syrup can be used in the corn-sensitive patient. Highly refined cane sugars and lactose are also nonanaphylactogenic forms of sugar.

3. At present we are engaged upon a study of the various common cereals and cereal foods. We may state that we have found, for example, that certain wheat cereals cooked for two to three hours, certain prepared cereals, pablum, and melba toast may be tolerated by the wheat-sensitive patient, whereas fresh bread, lightly tonsted bread, pie crust, certain crackers, and cookies are not tolerated.

4. If foods were thus classified, the pediatrician could prescribe the denatured foods and avoid the highly antigenic forms in the treatment of the asthmatic patient. In the absence of a list of nonallergenic foods, it is a safe procedure to cook foods in water and thus reduce their allergenicity.

The correction of the environment cannot be accomplished simply by removing the child's pillow and mattress, for example. All articles in the home which contain similar stuffings must be eliminated. Certain articles of furniture which cannot be discarded may, if properly reupholstered, prove harmless to the patient.

A word about drug therapy. Never give morphine. Give adrenalin in doses not larger than 2 or 3 minims. The inhalation of 1:100 solution of adrenalin has not been found valuable with children. Atropine is excellent. Ephedrine has its value.

I believe it not amiss to express concern about the present attitude of physicians towards allergy, especially their scepticism with respect to our knowledge and the possibilities of a favorable outcome of treatment as outlined. A case cannot be referred to an allergist merely for a diagnosis. The pediatrician must have a thorough understanding of the problems involved before he can treat the asthmatic child intelligently. I must remind you that I, too, am a pediatrician. It is true that our knowledge is still incomplete, but the situation is not discouraging. Each case requires individual study and treatment. Unfortunately you cannot obtain a brilliant result in every case by the simple eradication of a single offending substance. I advise you not to undertake treatment unless you are assured that the patient will remain under your care for at least a year. Many a patient who is apparently not progressing favorably will suddenly begin to respond to treatment after a period of several months. Constant observation, constant questioning, retesting, if necessary, will bring to light new and unexpected evidence. Attention must be focused on the patient's general metabolism and upon psychogenic and hygienic factors. Above all, treat the patient, not the allergic condition alone.

The facts that every tenth person has a fixed allergy and that at least 50 per cent of individuals suffer from minor allergies make it incumbent upon us to pursue our studies in this field and make it part of pediatrics.

DR. J. A. WHEELER (NEWTON, KAN.).—At the University of Kansas we have thought that asthma was possibly a germ plasm transmission.

CHAIRMAN RATNER.—The evidence for this concept is hypothetic and not proved.

DR. J. A. BIGLER (HIGHLAND PARK, ILL.).—What is the difference between familial transmission and inheritance in allergy?

DR. SCHMIDT.—The relatively high incidence of *antecedent* family history would suggest that the disease is familial. Proof of inheritance would depend primarily on studies of cases grouped according to *parental* history.

I do not believe that published data yet provide proof of the inheritance of susceptibility to allergy, but were such proof established it would not lead to a defeatist attitude, but to a possibly more fruitful attack on the question of *clinical manifestation* of the *inherited susceptibility.*

CHAIRMAN RATNER.—To conclude that a human affliction behaves as a Mendelian character requires courage that very few good geneticists will assume.

DR. K. BAIN (ST. LOUIS).—In a paper on the Elliott family they were able to trace 60 per cent of the descendants who had hay fever.

CHAIRMAN RATNER.—That is not necessarily hereditary; it is a familial occurrence of an acquired condition.

DR. MINNOLA STALLINGS (SAN FRANCISCO).—Since the Elliott family was an educated group, there was an unusual chance to get good and accurate information. I think the paper is a good, outstanding one.

CHAIRMAN RATNER.—I am familiar with Smith's paper on the Elliott family. It was an interesting paper, but Smith did not conclude that the condition in the family was inherited. She merely concluded that there was a high family incidence. Such a family, we have learned, only occurs in 0.4 per cent of all families studied. It is therefore largely fortuitous and not the rule.

DR. WM. B. MCILWAINE (PETERSBURG, VA.).—Do you mean to eliminate inheritance completely as a factor in allergy, or would you abolish it temporarily as a working hypothesis?

CHAIRMAN RATNER.—I do not believe that inheritance per se has been proved to play a significant rôle in allergy. Allergy is acquired like any other disease resulting from an invasion into the body of an antigenic substance. Serum sickness is not thought to be inherited, yet it presents all the characteristics of allergic diseases including such prominent features as a positive skin test and Prausnitz-Küstner antibody. Allergy can be prevented and successfully treated for the present. This should be our main concern.

DR. E. J. LAMB (SANTA BARBABA, CALIF.).—What percentage of your patients with allergy during the course of examination have shown endocrinopathies?

CHAIRMAN RATNER.—I cannot cite figures. We do have cases in which x-rays of the wrists show delayed ossification, in which case thyroid therapy is of value. I have found it especially useful in cases with dry skin, vasomotor rhinitis, and mucous colitis.

DR. STEVENS.—Although I have had little experience in this respect with children, adult females frequently have severe asthma caused by foods or by inhalants just prior to the menstrual period, and at no other time. Theelin properly administered will prevent this asthma in some patients. Urticaria due to low temperatures may also occur at this time and also in some patients with an associated low metabolic rate. Thyroid does not often help even though the metabolism is low.

DR. C. R. BROWN (ARLINGTON, N. J.).—Is feeding the infant other foods during the colostrum period of nursing likely to produce sensitivity in the child?

CHAIRMAN RATNER.—The permeability of the gastrointestinal tract in the newborn is so great that a state of sensitivity may be developed due to absorption of native proteins. I think evaporated milk should be used and not fresh cow's milk. There should be no feeding of raw milk during the colostrum period.

DR. BIGLER.—What about feeding lactic acid mixtures during infancy with the idea of eliminating the possibility of allergy during later childhood? This is recommended by some Eastern allergists.

CHAIRMAN RATNER.—Raw lactic acid milk is the most allergenic form of milk. If you are referring to acidified evaporated milk, that is different, for with such milk, allergy to milk proteins can definitely be prevented.

DR. WM. E. SINCLAIR (ORLANDO, FLA.).—Which do you think are the common foods that cause asthma, and how would you proceed to desensitize a child to them?

CHAIRMAN RATNER.—The most common food offenders are milk, egg, and wheat. This of course does not preclude the possibility of a child's being sensitive to any other foods. The problem of the denaturation of foods is one of vital importance to the pediatrician. In the single factor of heat we have a most powerful weapon for combating the deleterious effects of foods that are offending substances in the asthmatic case. In the milk-sensitive patient evaporated milk can be used, both as a beverage and in the preparation of foods, particularly if the child is sensitive to the lactalbumin or lactoglobulin fraction. Dry milk, pasteurized milk, and acidified raw milk are all highly anaphylactogenic and cannot be used for the milk-sensitive child. An egg boiled for half an hour is usually well tolerated by the egg-sensitive patient. Wheat that has been subjected to high and prolonged heating—whether a cereal or a breadstuff—can be tolerated by the wheat-sensitive case. Heat in the presence of water over prolonged period apply to any coagulable good protein tends to denature it. An interesting point about raw soluble proteins in foods is that they may escape digestion and enter the circulation through the permeable intestinal wall and thus produce allergic reactions; whereas heated, coagulated proteins are not absorbed as such but are attacked by the digestive enzymes and broken down into harmless polypeptids and amino acids. If a child is sensitive to ovomucoid (egg) or casein (milk), the problem is more complicated because heat does not change their antigenic properties.

DR. GEO. J. FELDSTEIN (PITTSBURGH, PA.).—Would you use goat's milk in cases of failure with evaporated milk? I should like to recite the case of a small infant who showed symptoms of shock when first given cow's milk; we tried evaporated milk without success. The signs of sensitivity were cleared with the use of evaporated goat's milk; at eight months the child was put on Carnation milk; and at one and a half years we put it on boiled milk. The child can now tolerate raw cow's milk. The skin is smooth and clear.

CHAIRMAN RATNER.—If the patient is so severely sensitive to casein as to react to evaporated cow's milk, then some other substitute may have to be sought; but in such a case, goat's milk—either raw or evaporated—will not help because the casein fractions of all milks are chemically and biologically related. This, therefore, was probably a case of extreme sensitivity to the whey proteins; in such cases I have had success with the judicious use of a good evaporated milk, without recourse to goat's milk.

DR. I. BINDER (PHILADELPHIA).—What is the rôle of calcium and phosphorus? Is there any study on phosphorus in the treatment?

CHAIRMAN RATNER.—There is no lowering of calcium or phosphorus levels in allergy.

DR. JOS. W. EPSTEIN (CLEVELAND, OHIO).—What effect does calcium have on the asthmatic child?

CHAIRMAN RATNER.—The use of calcium has been popular at certain times and has been discarded at other times. It is supposed to diminish the permeability of the membranes and quiet the nervous system. It must be given in large amounts to be efficacious, and for that reason is difficult to administer.

DR. LAMB.—Have you made any observations on reactions to combined food allergens when ingested within a limited time, which when taken individually and at greater intervals do not produce any reactions? For example, I can take chocolate and strawberries individually and at widely spaced intervals without reaction, but if I eat them at the same meal, or at two successive meals, I have urticarial eruption.

DR. PHILIP H. SYLVESTER (BOSTON, MASS.).—I think I have an instance which also illustrates this. A patient who never reacted to lobster or green corn taken separately reacted with asthma and urticaria when the two foods were taken together. This was corroborated by repeated experimentation with the patient.

CHAIRMAN RATNER.—In the case of reactions from combinations of foods, it is possible that an increased permeability of the intestinal wall at such times permits the passage of undigested proteins with consequent allergic symptoms, whereas, when these foods are taken singly, there may be less undigested protein and a lesser permeability. It is, however, fortuitous, and I believe is not related to the combination of foods.

DR. STEVENS.—It may be the result of summation. I know of a patient who reacted with hives and urticaria when clams and alcohol were taken together but had no reaction to clams otherwise. The alcohol may modify either the gastrointestinal tract or the skin.

DR. LAMB.—How often do you see cases of asthma due to thermal causes?

CHAIRMAN RATNER.—I believe thermal conditions are complementary; the excitant is specific.

DR. McILWAINE.—You seem to be fond of evaporated milk. Do you ever find it necessary to have recourse to sobee or other similar substitute for cow's milk?

CHAIRMAN RATNER.—I prefer evaporated milk to sobee or any other substitute. Evaporated milk serves not only as a substitute for raw cow's milk, but at the same time helps build up a tolerance to milk proteins. The introduction of sobee presents the possibility of a new antigen to which the child may become sensitized. Sobee is a powerful sensitizing substance and will sensitize a child in the same way that any other protein will. When one realizes that soy bean flour is being used today in conjunction with wheat flour in the preparation of common breadstuffs to a greater extent than one might believe, because of its high gluten content, the danger of sensitizing a child to it should be guarded against.

DR. JOSEPH WEINER (NEW HAVEN, CONN.).—Is there any danger of the sensitization of the newborn to cow's milk if complementary feedings of cow's milk are used until the breast milk flow is established, and the cow's milk is then discontinued until the child is weaned?

CHAIRMAN RATNER.—Your question is a most important one. The use of relief bottles in the obstetric nursery is one of the most frequent causes of milk sensitivity. No newborn infant should be given raw milk. If a relief bottle must be given, I recommend evaporated milk.

DR. WEINER.—Have reagins to cow's milk been shown in the infant?

CHAIRMAN RATNER.—Dr. Schloss's work answers this question; he has shown the presence of precipitins, complement fixation antibodies, and anaphylactic antibodies to cow's milk in the blood of both normal and athreptic children. The reagins and the above antibodies are identical, many investigators believe.

DR. A. G. DAVIS (UTICA, N. Y.).—You say that a 1:100 solution of adrenalin by intraoral spray is not particularly effective?

DR. W. E. VAN ORDER (CHATTANOOGA, TENN.).—You have stated that you do not recommend the use of 1:100 solution of epinephrine for inhalation in children. Would you not advise it for emergency use, and is it not safe if a doctor is not readily available?

CHAIRMAN RATNER.—When this method of treatment was first introduced, it was said to work in all cases and would be of benefit for use by the patient. I find it difficult to use with children. There may be serious consequences because of the rapid absorption through the mucous membranes in certain cases. There may also be acute gastric symptoms. It is not a controlled form of therapy and does not compare to the controlled use of small dose of 1:1000 solution of adrenalin given subcutaneously.

DR. WHEELER.—I had a patient who nearly collapsed in my office immediately after using 1:100 solution of adrenalin intranasally and intratracheally. I use the vaporizer with a small bulb which uses less force and consequently smaller doses of adrenalin.

DR. H. N. PRATT (BOSTON).—I am surprised to hear this about adrenalin intratracheally because in older children it works very well. If the mouth is rinsed after treatment one can avoid gastrointestinal symptoms. If the apparatus is faulty, then the droplets are too large. I think that after the age of seven or eight years a child can use it himself satisfactorily.

CHAIRMAN RATNER.—I think it is dangerous in the hands of the laity.

DR. PRATT.—I would limit it to the patients with severe asthma and those who can use it themselves—only after adrenalin hypodermically has failed. I tell mothers to use it with a very bright light so that they can see the cloud of spray. I have seen no severe reactions.

DR. STEVENS.—Adults develop alarming symptoms. In adults who are reasonably intelligent if the spray is first used by the physician so that if the patient is especially susceptible or has a tendency to use too large doses at one time reactions may be avoided, a spray of adrenalin is often quite beneficial. The dangers of its inspiration must be stressed.

DR. SCHMIDT.—Inhalation of adrenalin has been ineffective where injection has been effective. Judgment has been reserved by the Council on its use for the time being because of the number of reactions which have been reported.

DR. E. S. PLATOU (MINNEAPOLIS).—Are reactions severe enough to discontinue the use of adrenalin inhalation? And what is the dosage? What is the treatment of the reaction?

CHAIRMAN RATNER.—I believe adrenalin inhalation should be discontinued, particularly because it is impossible to control the dosage. Severe circulatory and gastric disturbances that result from its use add unnecessary disturbances to a child already overtaxed with his asthma. The treatment of the reaction is symptomatic.

DR. JEROME GLASER (ROCHESTER, N. Y.).—You have expressed your disapproval of morphine; how do you handle the child who does not react to adrenalin?

CHAIRMAN RATNER.—I believe it is a criminal offense to give morphine in an attack of asthma; it is the largest single cause of death during an acute attack.

DR. GLASER.—What about the use of x-ray?

CHAIRMAN RATNER.—X-rays should not be used as a therapeutic agent because of the possible deleterious effect on growing structures.

DR. GLASER.—What do you think of lipiodol?

CHAIRMAN RATNER.—Lipiodol appears to me to be unnecessary in childhood asthma, and, as a matter of fact, it has been shown to be of doubtful value in adults.

DR. FELDSTEIN.—You have said that x-ray is not indicated. I have used it successfully to shrink membranes in cases of antral infection and enlargement of tracheobronchial lymph nodes.

CHAIRMAN RATNER.—If you have a case that is complicated by other factors and if you have ruled out true allergic asthma, you are justified in seeking other treatment. In ruling out conditions that produce pressure on the trachea and larger bronchi, x-ray serves as an important diagnostic procedure. If one is dealing with enlarged glands or a tumor mass in the mediastinum, x-ray therapy may be of great value.

DR. HUGH LESLIE MOORE (DALLAS, TEXAS).—I would like to ask what your feeling is concerning homiodin as a preventive measure. It is a preparation for hypodermic use.

CHAIRMAN RATNER.—I do not know the preparation, but hydriotic acid has been used for many years in the treatment of asthma with some value, and iodide therapy in general may have some effect in the chronic case.

DR. STEVENS.—Has not potassium iodide been used effectively? I believe a patient is better off with fewer drugs. Helium may be helpful. Referring to a question which was raised with respect to morphine, may I say that we have seen cases of respiratory collapse following administration of morphine.

DR. ALFRED D. BIGGS (CHICAGO).—What do you think of sealed tubes put up by Abbott, which are allergens in liquid form?

CHAIRMAN RATNER.—Do you mean the pollens?

DR. BIGGS.—No, all allergens that are commonly used for the scratch test.

CHAIRMAN RATNER.—I do not think they are as good as the dry antigens; they deteriorate more quickly.

DR. EPSTEIN.—Should a pediatrician study allergy, or should allergy be a specialty apart?

CHAIRMAN RATNER.—As you know, I am a pediatrician, and I believe that it is quite clear that allergy is an integral part of pediatrics and that all pediatricians

should think in terms of allergy. Especially is this true when the first formula is prescribed and new foods are subsequently added. The pediatrician must be aware of the many allergic manifestations that present themselves in respiratory, dermal, and intestinal forms, and become an integral part of many infectious conditions, both acute and chronic.

Almost all adult allergy has its inception in childhood, and a faulty perspective of these conditions is too common in the early stages.

Pediatricians such as von Pirquet, Schick, Moro, Schloss and many others have added fundamentally to our better understanding of these conditions, and it is up to us to further this knowledge.

Hay Fever in Children

DR. SCHMIDT.—A curve of the age of onset of hay fever reveals that the most frequent period of onset is toward the end of the first decade and during the second decade of life. About 10 per cent of hay fever has its onset in the first 5 years of life.

About one-fourth of children with hay fever enter the clinic with an entirely unrelated complaint, and it is in these cases that a careful inquiry into history reveals the presence of a seasonal rhinitis not otherwise referred to by the informant. Since only about a third of children with hay fever have a past history of allergy, a negative past history by no means militates against a diagnosis of hay fever.

Intracutaneous tests, as in adults, manifest a high degree of specificity. In this group only one patient exhibited a false negative reaction. A number of patients reacted positively to pollens which seemed to have no relationship to clinical symptoms, but in some cases these patients later developed hay fever during the season of pollination in question.

The plan of treatment employed in this series was the perennial method, and the maximum dosage tolerated and usually reached did not differ from that in adults. In accordance with Rackemann's findings, no correlation could be found between maximum dosage and success of treatment.

An attempt to gather data relating to the underlying mechanism of hay fever, which might have bearing on Rackemann's concept of an optimal course of treatment for each patient, has been made in 28 hay fever patients at New York Hospital. Titration of antibody by a technic described by Lippard and Schmidt revealed that passive transfer antibody titer tends to remain constant in the absence of the patient's contact with pollen and to rise after a course of pollen injections. A high preseasonal titer is apparently related to protection against clinical manifestations.

Complications of hay fever include first, other allergic manifestations, especially asthma. Since only 13 per cent of these 90 children developed this complication, whereas a much higher percentage of adults manifest asthma with hay fever, early diagnosis and treatment may well decrease the incidence of asthma in later childhood and adult life. Sinus involvement is a frequent complication but often tends to improve with successful specific treatment of the pollen hypersensitivity. Successful treatment of hay fever is often followed by a diminution in the frequency of winter colds.

DR. McILWAINE.—You have spoken only of the simplest methods of testing. What do you think of testing the mother instead of the child?

DR. SCHMIDT.—Passive transfer is useful when the child is apprehensive or combative or the skin unsuitable for direct testing. The exact significance of circulating antibodies cannot always be appraised. For the time being, direct testing is the method of choice.

DR. McILWAINE.—We should do away with the term hay fever; the patient is not sensitive to hay, and it is not fever; the term pollen allergy should be used.

DR. SCHMIDT.—I agree with you that the term pollen allergy is more suitable in describing this condition. It is, however, very difficult to change common usage.

DR. GLASER.—What is the youngest age at which you have started hay fever treatments?

DR. SCHMIDT.—Two and one-half years. If there is a definite history of rhinitis in the first year of life, treatment should be delayed until a positive diagnosis is established. I have heard of a child, 18 months old, who was so treated.

DR. MAURICE T. BRIGGS (LYNN, MASS.).—Will you describe your technique for scratch test?

DR. SCHMIDT.—A break is made in the skin—we use a Hagedorn needle. The dry protein is applied to the scratch with a sterile toothpick, and a drop of N/10 NaOH used to moisten it and rub it into the scratch. In hay fever the scratch test is almost as good as the intracutaneous, except that the intracutaneous test is performed more quickly and may be the choice in a busy clinic; otherwise there is little choice between them.

DR. BRIGGS.—What would you regard as a positive reaction?

DR. SCHMIDT.—That depends entirely on the individual case; you must estimate the degree of reactivity of each patient.

DR. VAN ORDER.—Do you see any delayed reactions; how soon after the test do they occur, and what is their significance?

DR. SCHMIDT.—In one instance a silk-sensitive patient exhibited a delayed tuberculin type of reaction. This question needs investigation. We cannot now say what the significance is.

DR. NORMAN A. POKORNY (SPRINGFIELD, MASS.).—May not there be other physical factors concerned in pollen allergy? Do you not find in cases which are due primarily to pollens that at various periods the patient will have a bad day which appears to have no relation to his specific problem?

DR. SCHMIDT.—Yes, although the concentration of pollen primarily determines the severity of symptoms, physical factors also play a part. For example, when the temperature is high, the humidity low, symptoms are generally severe. On the other hand, when patients are in a filtered chamber, it is said that an increase in humidity aggravates symptoms.

DR. LOUIS A. KOCH (BROOKLYN, N. Y.).—Dr. Schmidt showed us charts giving the pollen titer in certain children who had hay fever and others who had been treated for hay fever. Are these slides in print yet? I also noted that in your slides some children who had been treated with smaller amounts, and others with larger amounts. What determines how much a child should have? Do you agree with Dr. Rackemann's advice to use all of the antigen you can safely give? Is it your experience that treatment with commercial products is probably too inadequate?

DR. SCHMIDT.—The technique for determining the pollen titer has been published in the *American Journal of Diseases of Children*. All of our patients were not pushed to the limit of their tolerance. I also feel that the dosage in commercial sets is often inadequate.

DR. VAN ORDER.—What is your explanation of the etiology of vernal conjunctivitis?

DR. SCHMIDT.—The etiology of vernal catarrh is unknown.

DR. P. W. BEAVEN (ROCHESTER, N. Y.).—What is the value of machines which are designed to filter out the pollen in the air of a room?

CHAIRMAN RATNER.—Their effect is only palliative. To give a pollen-sensitive child a good night's rest may help to make the following day a little easier; unfortunately, one cannot keep the patient in such an environment throughout the season.

DR. GLASER.—Is there any hope of getting earlier and more permanent immunization if done at any early stage?

DR. SCHMIDT.—There is no evidence that there is any correlation between duration of symptoms and success of treatment; early treatment may prevent complications.

CHAIRMAN RATNER.—Referring to Dr. Glaser's earlier inquiry with respect to the earliest age at which hay fever treatments should be started, may I say that it seems to me wiser not to start treatments on a child of 1 or 2 years; I prefer giving palliative treatment, getting the child to the seashore out of the pollen-laden environment, until the child is older and hay fever definitely established. Too early treatment may heighten the sensitivity.

DR. SCHWARTZ.—In the presence of definite pollen sensitivity, do food sensitivities—as established by leukopenic index—have any importance?

DR. SCHMIDT.—I have rarely used the leukopenic index; it may have a certain value, but limited.

DR. WM. PANITCH (NEWARK, N. J.).—What is the present opinion of the relation of seasonal vernal conjunctivitis to the pollen group, and what has been the result of pollen treatment? Is this purely a local manifestation of hay fever, and have these cases been followed by other allergic manifestations?

DR. SCHMIDT.—If one excludes the characteristic conjunctivitis of hay fever, the syndrome called vernal catarrh is an often associated but not necessarily related concomitant of hay fever. Relief of the latter by pollen therapy does not improve the former.

DR. R. E. PRAY (FARGO, N. D.).—How many pollens can be used in one mixture in treatment?

DR. SCHMIDT.—The related grasses are combined, as are the ragweeds. But combinations of ragweed and grasses are not used because they prevent independent variations of dosage.

DR. O. E. BARBOUR (PEORIA, ILL.).—Is there a satisfactory cure for vernal conjunctivitis?

CHAIRMAN RATNER.—There is no satisfactory cure. It seems to be a part of an allergic syndrome. These cases are very baffling and may be due to infection.

DR. WHEELER.—What is the relation of food to results and titer? When does hay fever develop?

DR. SCHMIDT.—The peak incidence is during the second decade and the last half of the first decade. The ketogenic diet was used on two patients. We do not

feel justified in using the diet to the exclusion of protein treatment. Ingestion of food to which an individual is sensitive also is followed by a rise of passive transfer antibody titer. Here also, as in the case of pollen sensitivity, high titer is apparently related to protection from clinical manifestations.

DR. DAVIS.—How about the ketogenic diet with ammonium chloride and acid?

CHAIRMAN RATNER.—We have worked on this, and the results were inconclusive. We have been using a low base diet with good results. The giving of hydrochloric acid may have some value. I have heard that a high alkaline diet also gives good results.

DR. STEVENS.—Acidifying diets and the use of acids are equivalent physiologically to a high vitamin D intake, which mobilizes calcium. Neither seems beneficial. Many of the statistical data compiled showing beneficial results in hay fever from these therapeutic measures were uncontrolled and failed to take into account the fact that the severity of hay fever varies from year to year so that accurate analysis must be made on an average of several years of treatment.

CHAIRMAN RATNER.—Estivin, popularly used for eye symptoms in hay fever, has an acid reaction; the mucous membranes are relieved probably because of this acid reaction.

DR. PLATOU.—Is there any evidence to suggest that antibody titer remains high after the pollen season?

DR. SCHMIDT.—There appears to be a decrease in titer after the termination of the season of pollination and the cessation of treatment. The patient is resistant when the titer is high.

DR. M. K. WYLDER (ALBUQUERQUE, N. M.).—Personally, when 20 years old, I had an onset of allergy which developed when I went to Albuquerque. I was sensitive to cottonwood, juniper, and thistle. By using diet and injections, I can remain free from symptoms, but if I break the diet, the symptoms return.

DR. PRATT.—The removal of other substances to which the patient is sensitive helps in the treatment with pollens. Some patients can tolerate the substance to which they are sensitive outside of the pollen season but not during the pollen season.

DR. E. P. RUSSELL (BERWYN, ILL.).—I have such a patient, a boy who can eat eggs outside of the ragweed season, but not during the ragweed season. He immediately develops an asthma if eggs are eaten during the season.

Infectional Asthma in Childhood

DR. FRANKLIN A. STEVENS.—Many children pass through a period during which they are susceptible to severe respiratory infections. These infections appear to be an abnormally prolonged and severe secondary bacterial phase of the common cold. Usually such infections are not accompanied by asthma, but in some children the severity of the infections increases with each attack until asthma occurs; subsequently asthma becomes a part of the symptomatology of the succeeding infections. Such severe infections occur most commonly in families subject to hay fever and asthma and probably are the result of environment as well as an inherited immune response less effectual against infection than that found in normal children. Some children apparently become immune as they grow older but the asthma and infections may continue into adult life.

In most respects the cultures from the throat and nose and from the sputum of one of these patients with repeated attacks of asthma resemble those found in acute

colds. Although the same bacteria are found in successive attacks if the patient happens to have a chronic focus infected with these bacteria, usually the flora of the nasopharynx and sputum of these patients varies greatly at different times. This variation is the result of the acquisition of new bacteria from time to time from contact with other patients with respiratory infections and the extermination of some strains previously present in the throat. Usually, even though an infected focus is present, the flora changes considerably within a few months. These variations in the flora are reflected in the cutaneous reactions to the bacteria, which also show continual variation. Reactions to some of the upper respiratory bacteria will disappear, and reactions to others will appear within a few months. Some time elapses between infection with a bacterium and the appearance of the corresponding cutaneous reaction, and then the reaction to the bacterium may persist long after the infection has ceased and the bacterium causing it has been exterminated. For this reason to correlate cutaneous reactions with the cultures is usually difficult unless cultures and skin tests are made at frequent intervals in series; even then, the mechanism and the relationship of the reactions obtained with bacteria to the asthma are not clear. Apparently, from studies made so far, successive attacks may be due to different bacteria. To determine which bacteria will be responsible for future attacks has been impossible.

Theoretically, because these children are seemingly unable to establish a normal immune reaction to respiratory infections, a procedure similar to the immunization against ragweed sensitization should be carried out. The preparation used should contain bacteria from cultures of the nasopharynx as well as other pathogenic bacteria ordinarily found in the populace at large during the winter months. Satisfactory results have been obtained with preparations made according to this method.

DR. S. R. KALISKI (San Antonio, Texas).—I have seen a child sensitive to wool and wheat. He could take wheat in any amount if he stayed away from wool and vice versa. If he took wheat and was exposed to wool, he would develop symptoms and marked rhinitis with high eosinophil count of the nasal secretions.

DR. WHEELER.—What is a cold and what is the yardstick to use to differentiate between a cold and allergy?

DR. STEVENS.—The mucous membrane changes which include bogginess, paleness, swelling, with a thin, clear mucoid discharge full of eosinophils are present in allergy. That same person during the winter with a cold has a red, inflamed mucous membrane with a secretion that contains leucocytes and neutrophils, unless he is similarly sensitive to bacteria.

DR. M. G. PETERMAN (Milwaukee, Wis.).—What is the distinction between asthmatic bronchitis and bronchial asthma?

DR. STEVENS.—There is essentially no difference. If the bronchitis or asthma is caused by sensitization to some pollen, food, bacteria or inhaled substance, the terms may be used to indicate the main point of localization of the clinical effects of the sensitization. In asthmatic bronchitis the symptoms are mostly bronchial with little spasm. In bronchial asthma there are definite symptoms of spasm of the smaller bronchioles.

DR. WEINER.—In the case of a child who develops asthma with infection, but in whom infections do not always precipitate asthma, and who at the same time is sensitive to ragweed for which he is being treated, would you suggest treating him for both conditions?

DR. STEVENS.—A patient who is susceptible to both infection and ragweed should be treated for both. We do find, however, that often the treatment of the ragweed susceptibility alone is sufficient to ameliorate the susceptibility to infection.

DR. McILWAINE.—In asthmatic bronchitis what vaccines do you use?

DR. STEVENS.—In my paper I have shown the reasons why the bacterial preparation used should be made from an autogenous culture of the nose, throat, and sputum, and why other bacteria which commonly invade the nose and throat during the winter should be included as well. After using nonspecific vaccines, catarrhal vaccines, autogenous vaccines, and preparations of autogenous bacterial filtrates, I have found that the best results are obtained when autogenous filtrates are made and then filtrates of other upper respiratory pathogens are added to the mixture. However, if results are to be obtained, this preparation must be used as persistently as any other antigen used for the treatment of hay fever or asthma.

DR. SINCLAIR.—Can vaccines be taken by mouth?

DR. STEVENS.—While vaccines such as typhoid vaccine by mouth may immunize against a disease such as typhoid fever in which infection normally takes place through gastrointestinal tract, the evidence for similar immunization against upper respiratory infection is not at all conclusive.

DR. M. C. FIELD (BROOKLYN, N. Y.).—In immunizing with pollens, is there any difference between intracutaneous and subcutaneous injections?

DR. STEVENS.—At the present time I have no statistical data nor do I know of well-controlled clinical data comparing the two methods of injection. Intracutaneous injections may be advantageous in that the antigen is absorbed more slowly.

DR. PRAY.—What is the relation of the tubercle bacillus to asthma in the individual with tuberculosis and asthma?

DR. STEVENS.—Although asthma occurs in patients with tuberculosis, whether this asthma is caused by the tubercle bacillus or by bacteria causing secondary infection is difficult to decide.

DR. DAVIS.—What is the value of humidity in the home to stop upper respiratory infections?

DR. STEVENS.—Data on this point are not available. Humid atmospheres are usually unsatisfactory for asthmatic patients, while dry atmospheres seem to benefit those where the asthma is due to infection alone. Most respiratory infections due to bacteria occur in seasons when the weather is both cold and damp and subject to sudden changes in both temperature and humidity. Even though a home might be properly tempered, unless the patient is continually confined, he would still be subjected to the deleterious effects of the weather outdoors.

DR. WHEELER.—Is it the temperature change or the barometric change which makes a difference in upper respiratory infections? Does pertussis have any influence on the development of allergy?

DR. STEVENS.—The effects of temperature change and barometric change are so often related that clinically it is impossible to determine which affects upper respiratory infections. Asthmatic patients kept at constant temperatures and humidities are sometimes affected by barometric changes.

Pertussis in children is often followed by asthma. In fact any upper respiratory infection may, because of the inflammatory reaction resulting, bring out clinical sensitizations to bacteria or inhaled allergens.

DR. PRATT.—Dr. Steven's paper was a beautiful piece of control work and bears out my own observations. The same organism seldom initiates future attacks. The positive skin reaction to bacteria has the same relation as the tuberculin test in those individuals who have been infected. There is no question that upper respiratory infections will precipitate an attack of asthma in a child who is usually atopic. This may be due to the change in the permeability of mucous membranes so one has to be careful in thinking that attacks are really due to the bacteria.

DR. STEVENS.—It is apparent that the mechanism of asthma caused by injection differs from that caused by the common allergenic proteins. The asthmatic response having been established in a child occurs after a wide variety of stimuli. These stimuli may be mechanical (inert dust), physiologic (increased circulation following excitement or exercise) or physical (the effect of breathing cold air). Whether the asthma caused by upper respiratory infection is the result of the mere stimulation of the bronchi by the inflammation of the infection or the result of increased reactivity of the respiratory tract to the bacteria is open to question. Clinical and experimental evidence suggest both play a part.

CHAIRMAN RATNER.—Gentlemen, I am certain that this discussion could be carried on for several more hours and with profit to all of us, but I regret that our time is up. We thank you for your close attention and deep interest.

PAUL K. BEAVEN, Secretary,
Rochester, N. Y.

MEETING OF REGION I OF THE AMERICAN ACADEMY OF PEDIATRICS

The meeting of Region I last November was very well attended and represented the largest gathering of pediatricians ever assembled in Boston. A number of guest speakers commented on the character of the audience, which consisted of a very large group of young, enthusiastic pediatricians.

The outstanding feature of the program was the symposium on vitamin C. We were fortunate to have in Boston such a large group of men actively engaged in work on this subject, and the audience took away a great many practical suggestions from these discussions. It seemed wise to the committee to emphasize in the program subjects of general medical interest and to introduce speakers outside the field of pediatrics. Dr. Fuller Albright aroused particular interest with his clinical description of a syndrome characterized by osteitis fibrosa, pigmentation, and gonadal dysfunction. We were fortunate, also, to have Dr. Soma Weiss, who discussed the late stages of pyelitis after this infection in the young had been discussed by Dr. Allan M. Butler. This served to emphasize the great importance of follow-up studies after urinary infections in childhood.

There were no round table presentations, but instead informal clinics were held with limited attendance. The greatest interest was shown in the discussions on acute rheumatic fever at The House of the Good Samaritan under the guidance of Dr. T. Duckett Jones.

A luncheon meeting was held for the state chairmen, and all except two states were represented. It was recommended that the next regional meeting be held in Rochester, New York.

Fundamental Pathology of Vitamin C

S. Burt Wolbach, M.D.

Scorbutus is characterized as the inability of supporting tissues to produce and maintain intercellular substances. Whatever other rôles vitamin C plays in the chemistry of the body, it is indispensable for the formation of all intercellular substances, the collagen of all fibrous tissue structures, the matrices of bone, tendons, and cartilage, and possibly all nonepithelial cement substances including that of the vascular endothelium. These conclusions were reached through histologic studies of human infantile scurvy and largely through studies of the histologic sequences of progressing scurvy in growing guinea pigs and of the repair following administration of vitamin C in natural forms or in crystalline form, ascorbic acid or cevitamic acid.

The reparative proliferative powers of epithelial cells, endothelial cells, fibroblasts, and odontoblasts are not interfered with. The mechanism of calcification is not interrupted.

The gross and microscopic pathology of scorbutus may be accounted for entirely on the basis of the above characterization.

Failure of intercellular materials, and therefore mechanical weakness, accounts for the occurrence and distribution of hemorrhages in scorbutus. Even the petechial hemorrhages of the skin are determined by the sites of the erector pili muscles. Naturally, all the phenomena of scurvy are most pronounced in growing individuals where continuous formation of intercellular materials is going on in important loca-

tions. For example, normal growth sequences are maintained in endochondral bone formation, but inasmuch as cells concerned in normal bone formation cannot make bone matrix, there is a rapid solution of the continuity at the epidiaphyseal junctions—hence infraction and traumatization.

Use and Abuse of Vitamin C Determinations

Otto A. Bessey, Ph.D.

The development of the chemical method of analysis has given a great stimulus to the study of vitamin C nutrition and physiology. The widely used indophenol titration technique, first developed to guide isolation operations, has been useful in a number of problems: in obtaining a thorough knowledge of the distribution of vitamin C in plant and animal tissues and how it varies with storage, handling, cooking, canning, and other processes important in relation to the general food supply, by its application to blood and urine analysis to determine the state of vitamin C nutrition, the daily requirements of the individual, and how this varies in health and disease. It has been helpful in showing that the breast-fed infant of a normally nourished mother receives from 20 to 40 mg. of ascorbic acid daily from birth and in establishing the fact that a larger proportion of the population than is generally realized has a subclinical vitamin C deficiency.

Relation of Vitamin C Deficiency to Dental Lesions

Paul E. Boyle, M.D.

Tooth formation in the guinea pig is affected by the scorbutic process in a similar manner and in at least as marked a degree as is bone formation. The essential findings are atrophy of the dentine-forming cells and cells of the tooth pulp with production of a collagen-deficient but calcified matrix. The width of normal dentine produced is proportional to the amount of ascorbic acid administered. During the last stages of acute scurvy, all formation of dentine ceases. In chronic ascorbic acid deficiency, the capillaries associated with the dentine-forming cells fail to occupy the position found in normal control animals. This may be due to lack of ability to form the cement substance of capillaries.

Enamel formation is not primarily affected by the deficiency.

Evidence from study of tooth germs removed at autopsy and clinical study of the teeth of children with previous hospital records of acute scurvy indicate that human teeth are much less affected than the teeth of the experimental animal. It appears probable that some arrest of dentine formation occurs. Uncomplicated scurvy is not a cause of enamal hypoplasia.

In both man and the guinea pig, normal ascorbic acid nutrition is essential for the maintenance of the tissues by which the teeth are attached to the jaws. Loosening of the teeth in ascorbic acid deficiency is the result of atrophy of the collagen-producing cells which govern production and maintenance of the tooth-suspending tissues. Such suboptimal ascorbic acid nutrition is an underlying factor in the production of the systemic type of pyorrhea.

Observations Upon the Vitamin C Content of Blood in Pregnant Women and Newborn Infants

Harold M. Teel, M.D.

The amount of ascorbic acid (vitamin C) in maternal blood tends to diminish as pregnancy advances. The amount in blood from the umbilical cord of the newborn infant is consistently greater than in the corresponding maternal blood. In general,

the difference between maternal and cord blood was most marked in those instances in which the amounts of ascorbic acid in maternal blood were least. The average amount of ascorbic acid in maternal blood during the first twenty-eight weeks of pregnancy was 0.72 mg. per cent; at the time of delivery, 0.54 mg. per cent; and the average value for blood from the umbilical cord at birth was 1.30 mg. per cent.

There was good correlation between independently taken dietary histories of vitamin C intake and the amount of ascorbic acid found both in maternal and in fetal blood.

This study indicates that during pregnancy women need more vitamin C than when at reproductive rest. Among patients of this clinic, when the diet was not influenced during pregnancy, both dietary histories and determinations of ascorbic acid in the blood indicated that the intakes of vitamin C were below optimum range or frankly deficient in more than half of the patients studied.

Growth and Development of the Visuosensory Mechanism

Theodore H. Ingalls, M.D.

Ascorbic acid nutrition is a relative term embracing several zones of vitamin depot between a protective saturation of the tissues and clinical scurvy. Even a saturated individual, when placed on a scorbutic dietary for three months, exhausts his tissue depots by a combination of excretion and metabolic processes.

Therefore it is advocated that the ascorbic acid supplement be added to the infant's dietary early in the neonatal period rather than after a delay of several weeks. In support of this viewpoint four instances of asymptomatic scurvy are cited which were demonstrated histologically in infants dying at the ages of 18, 26, 32, and 57 days, respectively. Further evidence is offered by the results of titration for ascorbic acid in the livers of a series of thirty-eight infants coming to autopsy. Of twenty-five babies dying before the age of 1 month, only one showed a reducing value of liver tissue less than 10 mg. per 100 gm. of tissue. Of thirteen infants dying between the ages of 1 and 4 months, seven showed such a low value.

Information as to the amount of vitamin C ingested daily by normal breast-fed infants was obtained by assay of mother's milk. It was calculated that the figure was in the neighborhood of 20 to 30 mg. of ascorbic acid per day. It is felt that this amount represents the desirable daily dose, and it is pointed out that amounts capable of preventing florid clinical scurvy may still be far below what is needed for perfect functioning of the organism. Both pasteurized cow's milk and pooled pasteurized human milk were found to be grossly deficient in vitamin C content.

Relation of Vitamin C Deficiency to Wound Healing

Thomas H. Lanman, M.D.

Vitamin C plays an important rôle in the healing of experimentally produced wounds in guinea pigs.

There may exist in human beings a degree of vitamin C deficiency that cannot be recognized by methods ordinarily used in physical examination.

It has been proved histologically and chemically that asymptomatic scurvy is far more common in infants and children than has been realized. Its existence in older patients, though not proved, undoubtedly occurs.

Evidence is presented that a partial vitamin C deficiency is of more importance in the healing of surgical wounds in human beings than has hitherto been appreciated. When a low ascorbic acid depot in a patient is found or suspected, the giving of ascorbic acid, as an aid to wound healing, seems amply justified.

Effect of Anemia on Bodily Function and Growth

Louis K. Diamond, M.D.

1. Observations on effect of anemia produced experimentally in white rats fed on iron-deficient diet. (Pure milk.)
   - A. Blood changes.
   - B. Bodily growth and weight.
   - C. Skin and hair.
   - D. Gastrointestinal tract. (Appetite, diarrhea.)
   - E. Heart.
   - F. Tendency to secondary infection.
2. Observations on effect of anemia in infants and children.
   - A. Blood changes.
   - B. Growth. (Height and weight averages compared with normal.)
   - C. Skeletal system.
     1. Long bones.
     2. Ossification of carpal centers.
   - D. Heart.
   - E. Gastrointestinal tract.
     1. Appetite.
     2. Gastric acidity and gastric function.
     3. Diarrhea.
   - F. Nervous system and brain.
   - G. Muscles.

Dehydration, Acidosis and Alkalosis

James L. Gamble, M.D.

The chief purpose of the discussion of these disturbances of extracellular fluid is to point out that the impairment of renal function which dehydration eventually causes contributes extensively to the development of the defects in the chemical structure of extracellular fluid which result in acidosis or alkalosis. The implication of this relationship between volume change and structural change is that in extracellular fluid disturbances of such severity as to require parenteral therapy, both dehydration and acidosis or alkalosis must be dealt with. The rational of the use of salt solution and of glucose solution is considered, and the requirement that both solutions be used is emphasized.

Chronic Pyelonephritis and Hypertension

Allan M. Butler, M.D.

During the past few years we have been impressed with two points in relation to chronic pyelonephritis. The first deals with the frequency with which renal failure and uremia are due to chronic pyelonephritis. Löhlein, Abt, Kretschner, Helmholz, György, Campbell and Lyttle, Longcope and Winkenwerder, Ellis, and others have called attention to the serious renal damage that frequently follows chronic renal infection. Mortality figures for pyelonephritis from the Infants' and Children's Hospitals based on the total number of cases so diagnosed without division into acute and chronic cases substantiate the seriousness of the prognosis. During a ten-year period 296 infants and 489 children with pyuria were treated on the wards of the hospital. The autopsied cases alone indicate a mortality among these patients with pyelonephritis under 2 years of age of at least 9 per cent and over 2 years of at least 3 per cent. These autopsy mortality figures are raised to a mortality of 20 per cent for infants and 4 per cent for children, if we include the patients with

pyelonephritis who died in this hospital but were not examined at autopsy. How much these mortality figures would be raised if they could be made applicable only to the chronic pyuria patients by subtracting the number of patients with acute pyuria from the total number of patients, and if all deaths out of the hospital were recorded, is not known.

Such reports, however, do not stress the frequency with which renal failure with uremia due to an antecedent pyelonephritis is encountered as compared with that due to a chronic nephritis. If the serious prognosis of chronic pyelonephritis is justified, then the greater incidence of this condition in childhood as compared to chronic nephritis would lead one to suspect that renal failure would be more commonly encountered following the former than the latter. Our figures support this rather strikingly. During the past ten years twenty-nine patients dying from renal failure and uremia were examined at autopsy. Twenty-six of these patients were proved to have had chronic pyelonephritis as compared at three who had chronic nephritis. Uremia from chronic nephritis, in spite of the almost certain course of the disease, is rare because the disease is rare. From the experience of this clinic, uremia in childhood should lead one to suspect a past history of pyelonephritis.

The second point deals with the relation between chronic pyelonephritis and hypertension. Ritter and Baehr, Weiss, Parker and Robb, Peters and coworkers, and Kimmelstiel and Wilson have observed hypertension early in pyelonephritis. More generally as reflected by Volhard, Schwarz, Longcope and Winkenwerder, Fishberg, and others hypertension has been associated with the contracted kidneys and the nitrogen retention that accompany the late stage of pyelonephritis. We have found no report of a serious hypertension occurring in the pyelonephritis of childhood before renal insufficiency was present. Amberg, in reporting 25 cases of hypertension in children, included five patients with pyuria or bacilluria but made no particular comment on this.

During the past ten years we have encountered fifteen patients who have had chronic pyelonephritis and hypertension over a period of years before there was appreciable diminution in kidney function. The average systolic and diastolic blood pressures in these patients, of whom six are dead and nine living, were, respectively, 170 and 115 mm. of mercury. Three of these patients ran a course typical of malignant hypertension with hypertension crises and death from cardiac failure before the occurrence of significant nitrogen retention. Though the hypertension preceded diminution in renal function in fourteen of these cases, there is no proof that it followed the pyelonephritis. But in one of these patients we know definitely that a unilateral pyelonephritis preceded a definite hypertension, cardiac enlargement and decompensation. Moreover, removal of the one infected kidney resulted in disappearance of the hypertension and cardiac enlargement. The urine has remained clear and the blood pressure within normal limits for twenty-two months. Subsequently, another patient on the services of Dr. Higgins and Dr. Barney at the Massachusetts General Hospital, who had a unilateral pyelonephritis and hypertension, had the one infected kidney removed and the hypertension was relieved. This patient's blood pressure has remained within normal limits for four months.

The clinical significance of the observations reported here is clear. Hypertensive cardiovascular disease may be associated with chronic pyelonephritis and relieved by removal of the infection.

This is not the place to discuss the relation between hypertension and urinary obstruction, circulatory disturbances in the kidney, and infection, but it is appropriate to state that a study of the pathology has revealed no explanation as to why some patients with pyelonephritis develop hypertension before renal insufficiency, while some develop it only after renal damage has become marked, and still others die in uremia with little or no hypertension.

The Late State of Pyelitis and Pyelonephritis as Seen in Adult Life

Soma Weiss, M.D., and Frederic Parker, Jr., M.D.

The purpose of this investigation was to ascertain the natural history of pyelonephritis ("pyelitis"). One hundred cases with necropsies, representing various manifestations and stages of the disease, were selected for analysis. The age of the youngest patient was 1 month and that of the oldest, 81 years.

As indicated by the histologic examination, pyelitis practically never exists without associated pyelonephritis. The disease is relatively frequently unilateral. Pyelonephritis is a disease of more common occurrence than glomerulonephritis. While pyelonephritis can be of (a) hematogenous, (b) ascending or (c) lymphatic origin, the analysis of the clinical course and of the structural characteristics of the kidney usually does not reveal the origin of the infection. In all types of pyelonephritis marked changes occur in the renal lymphatic system as well as in the nephrons. The inflammation in the lymphatics frequently affects the tubules, the glomeruli, and the arteries, but rarely involves the veins. The course of the infection and inflammation is strikingly variable. The acute process may heal after a short classical clinical course, or it may persist for years or for decades, during which the activity may be continuous or recurrent.

Chronic pyelonephritis results in gradual diminution of kidney structure and function. This is characterized mainly by progressive disappearance of nephrons, scarring, dilatation of tubules with atrophic epithelium, often filled with colloid casts, and peritubular and intratubular inflammation. The smallest kidneys (renal rickets) observed, weighing 20 gm. (single kidney), were found in the end stage of pyelonephritis of childhood. Functional tests indicate a progressively decreasing, though considerably fluctuating, kidney reserve and function.

The clinical course of chronic pyelonephritis has been well described by Longcope, Ellis, Peters and others. The diagnosis, if history of early infection is lacking, may be difficult as there may be long periods during which pyuria is not present. The presenting symptoms in the chronic or healing stage are often dependent on the associated hypertension and anemia. Vascular crisis, neuroretinitis, periodic elevation of the cerebrospinal fluid pressure, fluctuation in kidney function, and toxemia of pregnancy occur in the advanced chronic stages.

Both active and healed chronic pyelonephritis are frequently associated with arterial hypertension. Close relationship has been found between renal vascular changes and arterial hypertension. With increasing severity of hypertension an advanced degree of hyperplastic arteriolosclerosis, endarteritis proliferans, and necrotizing arteriolitis has been observed in various stages of the disease. In contrast to benign nephrosclerosis, hyaline arteriolosclerosis is rare in pyelonephritis. Study of the vascular lesions in various stages of the disease, within and outside of the pyelonephritic scars, and in instances of unilateral pyelonephritis indicates that changes associated with inflammatory processes (active or healed) and the degree of intravascular pressure play the main causative rôle. The factors involved in the vascular processes in pyelonephritis are quite similar to those active in the lungs in certain cases of advanced mitral stenosis with pulmonary hypertension (Am. J. Pathol. 12: 573, 1936). The vessels of other organs than the kidney, particularly in the young group (below 40 years of age), are relatively normal.

It is concluded that the various types of renal vascular changes observed play a rôle in initiating or accentuating arterial hypertension and in accelerating the vicious cycle of the disease. The hypertension in pyelonephritis is renal in origin. It has been estimated that pyelonephritis was present in from 10 to 20 per cent of the cases with "malignant hypertension."

Pyelonephritis, particularly in its chronic stage, should be considered as one type of Bright's disease. It is responsible for a group of cases in which chronic infection,

inflammation, and benign and malignant nephrosclerosis are present in various combinations. In rare instances pyelonephritis and glomerulonephritis are present simultaneously. Pyelonephritis is a disease of significance in obstetrics, pediatrics, and internal medicine.

Estrogenic Factors in Adolescence

Ira T. Nathanson, M.D., Charlotte Rice, and Joseph C. Aub, M.D.

Assays of the twenty-four-hour specimens of urine from sixteen boys and thirty-four girls between the ages of five to fifteen were carried out for the presence of estrogenic substances. Several determinations were made on younger children. In general, the amount present seemed to vary directly with the age of the patient, although the stage of physical development seemed to be more important than the chronologic age. Below the age of six, however, it was difficult to quantitate the amount of estrogenic substance, although its presence could be demonstrated. There was no noticeable difference in the excretion between males and females. Marked rises in the output of the estrogen were noted in children who seemed to be developing rapidly, especially at the time of puberty. The value of these determinations in the study of endocrine disturbance and disease in childhood is discussed.

Syndrome Characterized by Osteitis Fibrosa, Pigmentation, and Gonadal Dysfunction

Fuller Albright, M.D.

Ten cases of the syndrome were presented and the following characteristics of the syndrome were emphasized:

1. A disseminated osteitis fibrosa (both hyperostotic and hypoostotic) with a distribution suggesting a relationship between the lesions and nerve roots or an embryologic defect in the myotomes.

2. Areas of cutaneous pigmentation which have a distribution suggesting some connection between them and the bone lesions.

3. Sexual and somatic precocity, especially, if not only, when the disease occurs in the female sex.

The bone manifestations were likely to be mistaken for hyperparathyroidism and some of the differential points were discussed. Some remarks in regard to the possible etiology were made.

Laboratory Studies With the Virus of Poliomyelitis

James D. Trask, M.D.

Data were presented to show the difficulty and irregularity of recovering the virus of poliomyelitis in nasal washings of patients and contacts. Experimental poliomyelitis on cutaneous inoculation was described following section of the olfactory nerves.

Accordingly it seems unreasonable to accept as established that the nose is the natural portal of entry.

The Normal Development of Infants' Feet

William T. Green, M.D.

Pain as a result of foot strain is much less frequent in children than in adults, granting that the most common cause of so-called "growing pains" in the lower extremities has such an etiology. This depends in large part upon the long-retained static attitudes which the overweight adult is forced to maintain, thus provoking symptoms in instances where the structural weakness is already present. The me-

chanical arrangement and efficiency of the given foot depend upon its bony, ligamentous, and muscular structures which are in part inherited, but may be modified by disease, fatigue, shoes, supportive aids, exercises, and habits of locomotion. The evolution of the normal foot is traced from birth through the early years including the appearance of osseous centers. Since the incidence of distressing symptoms is minimal in childhood as compared to that of the adult, structural characteristics apart from symptoms merit therapy.

Growth and Development of the Visuosensory Mechanism

Theodore L. Terry, M.D.

A brief review of the salient features of embryonic development is given with particular reference to the production of important congenital defects of the eye.

The eye is comparatively large at birth. To attain adult size it grows proportionately less than the brain. Nevertheless, the eye is a very incomplete organ of vision at birth, and vision is necessarily very poor. Further differentiation of the retina, particularly in the region of the fovea, continues up to seven months. The retina, in spite of its relatively poor differentiation has little or no lateral growth, at birth its surface expansion being approximately that of the adult.

Embryonic defects in development lead to the production of primary and secondary colobomas, of the so-called glioma of the retina, and of the persistent fibrovascular nutritional membrane on the posterior surface of the lens. This persistent vascular membrane on the lens, often mistaken for the retinal tumor, may lead to unnecessary enucleation of the eye.

Myelinization of the optic nerve occurs about three weeks after birth in premature as well as in full-term infants. This suggests that nerve impulses of vision may stimulate myelinization.

The pathway followed by visual impulses from the various parts of the retina to the cortex is outlined.

Amblyopia in Children

Trygve Gundersen, M.D.

In the treatment of squint two problems exist: first, the correction of the deviation, and second, the prevention or correction of amblyopia. Amblyopia always develops if the squint is not frankly alternating and if the squint develops under five years of age. The younger the child, the more rapidly it develops, and the more rapidly it can be corrected. Amblyopia may be present in eyes which appear straight, but without binocular vision; hence the value of routine eye examinations in all children. The amount of squint has no relationship to the degree of amblyopia. Assume that amblyopia exists, or will develop, in all infants with squint. Vision can and should be tested between one and two years of age. Best treatment is occlusion of the normal eye, preferably continuous occlusion. May compromise in certain cases. Atropinization is sometimes effective when amblyopia is not marked. Hysterical amblyopia is usually bilateral and is seldom seen in children under ten years of age. It is usually easily diagnosed by a normal objective examination and careful field tests.

Growth and Development of Visuosensory Mechanism

Virgil G. Casten, M.D.

The extraocular muscles develop from the mass of mesoderm behind the eye and are present in the 20 mm. embryo. About this time, the oculomotor nuclei are developing in the midbrain. Important higher cerebral centers appear later. The

purpose of this neuromuscular mechanism is to move the eyes in order to see in three dimensions. Action of the elevator and depressor muscles of the eyeball gives the sense of position in the vertical plane. Lateral movements give the sense of position in the horizontal plane. The third dimension is supplied by the convergent-divergent movement which is very necessary and important for binocular single vision and fusion. The latter is present in man but not in the lower animals. Anomalies of binocular vision often result in strabismus.

Strabismus

Walter B. Lancaster, M.D.

Nature and Causes.—Combined effect of (1) a tendency to deviate usually innervational, rarely anatomical, never due to a "weak muscle," plus (2) ineffective fusion favored by visual defects, leads to amblyopia.

Diagnosis.—False vs. true strabismus; concomitant vs. paralytic; monocular vs. alternating; cover tests.

Treatment.—Of amblyopia ex anopsia by excluding the good eye, technique; of tendency to deviate when anatomical, by operation, when innervational by glasses and sometimes by operation; of ineffective fusion by orthoptic training aided often by operation, voluntary conscious control. Choice of time for operation, must not let patient become self-conscious because of danger of developing inferiority complex.

Refractive Errors in Children

Harry K. Messenger, M.D.

Every child is born with a refractive error, but not every child needs glasses. At birth, by a wise provision of nature, the eye is almost invariably hypermetropic. Its anteroposterior axis is too short for the formation of a perfect focus on the retina without the exertion of accommodation. Since hypermetropia of low degree can be readily compensated by accommodation, of which the young child has ample, it is of no consequence as a refractive error, and hence does not need correction. As the child grows, the anteroposterior axis lengthens both relatively and absolutely, and the eye tends to become emmetropic. Hypermetropia needs correction when it is great enough to interfere with clear vision, when it causes discomfort, when it cannot be compensated except by the expenditure of an undue amount of nervous and muscular energy, and when it is associated with internal strabismus.

Myopia is seldom if ever present at birth, and its prevention is a major problem for the pediatrician. The importance of dealing not with the eyes alone but with the whole child cannot be too strongly emphasized. Unfortunately there are many theories regarding the etiology of this distressing condition, but very little has yet been established by irrefutable proof. We need not concern ourselves in the unending argument whether glasses do or do not check the progress of myopia, but we can assert that every myopic child needs glasses. Without glasses he is reduced to living within a very small world, and his development and character are greatly affected.

A clear retinal image in the presence of astigmatism, which is perhaps the commonest of refractive errors, is not possible. Many cases of backwardness in children are really due to high astigmatism. The child is out of adjustment with the world because he has never seen it properly. Correction of all but the very lowest amounts of astigmatism is desirable at an early age.

A term now frequently met in ophthalmologic literature is aniseikonia, by which is meant a condition in which the size of the visual impression or image as received

by the brain is unequal in the two eyes. Lenses for the correction of this anomaly have been devised. It is undoubtedly true that the possibility of aniseikonia should be considered in cases of asthenopia not relieved by ordinary means, and the relation between aniseikonia and strabismus is being attentively studied at present. Though the question of aniseikonia is still, however, in its infancy, and few oculists are trained and equipped to prescribe iseikonic lenses, its importance must not be overlooked.

What Constitutes an Adequate Eye Examination in Children?

J. Herbert Waite, M.D.

The importance and the methods of winning the cooperation of the child in an eye examination were discussed. Inability to win such cooperation from the very young child, or from the overtimid child, in whom there is suspicion of abnormality of the eyes creates the necessity for administration of a general anesthetic for an adequate examination of the ocular media, fundus oculi, and ocular pressure.

Ways and means were outlined for gathering objective findings relating to the normal development, the maldevelopment, and the important diseases of the eyes of children. An evaluation of the subjective responses of the child in terms of central vision, peripheral vision, accommodation, and synergy of ocular muscles was made with the aid of statistical studies.

Factors Influencing the Incidence and Course of Otitis Media in Scarlet Fever

Conrad Wesselhoeft, M.D.

The discussion is based on an analysis of ten thousand cases of scarlet fever at the Haynes Memorial Hospital, Boston, supplemented by compilations derived from such sources in the literature as could be adjusted to charts and tabulations. Among 371,778 patients with scarlet fever, 46,343, or 12.5 per cent, developed otitis media suppurativa.

The incidence of otitis is influenced by season, being somewhat less frequent in summer than in winter. Climate appears to exert less influence on the incidence rate than it does on the morbidity of scarlet fever. In approximately the same periods covered it was 12 per cent in Boston, Los Angeles, Stockholm, and Rome.

The incidence according to the case rate by ages shows a constant decrease in the first year of life as compared to the second and third years. Thus it would appear that the high incidence in early life is not as dependent on the length and breadth of the Eustachian tube as it is on the vulnerability of the adenoids. Otitis media occurs equally in the two sexes.

Certain mixed infections definitely increase the incidence rate of otitis media in scarlet fever. Even scarlet cases which are diphtheria carriers have a higher rate, while diphtheria itself if superimposed on scarlet gives the highest rate. Measles offers much room for thought because it has much the same rate as scarlet fever. Since the hemolytic streptococcus is found in the aural discharge in both diseases, one must not be too ready to assume that the cause of middle ear suppuration in scarlet fever is always due to the etiologic agent of this disease.

Bilateral otitis media occurs in slightly more than half the patients in the first five years of life, and also in cases where certain other diseases are superimposed on scarlet fever, such as diphtheria and measles. The influence of symbiosis on the origin of otitis media in scarlet fever is stressed.

The *genus epidemicus* of scarlet fever as it pertains to middle ear involvement often loses much of its mystery when the factors which influence the incidence of this complication are brought to light.

Individual isolation of scarlet fever cases lowers the incidence rate, probably through protection from other strains as well as from mixed infections. Contrary to our expectations, in cases in which tonsillectomy has been performed prior to the scarlet fever, the incidence rate of otitis media is not lowered.

It is impossible to show that paracentesis exerts any influence in reducing the incidence of surgical mastoiditis. The best evidence available gives a negative answer. This does not mean that paracentesis is not beneficial in other ways. The early recognition of, and operation for, acute destructive and chronic suppurative mastoiditis conserves hearing, shortens the period of quarantine, and saves lives. This is of far greater importance than early paracentesis.

Early serum therapy in scarlet fever exerts only a slight influence in reducing otitis media.

Prontylin was given to 100 cases of scarlet fever during the initial febrile stage in the fall and winter months, 1936-1937, at the Haynes Memorial Hospital. As controls for this series, 100 cases were observed over the same months of the same ages, so that the average age in each group was ten and one-half years. No cases were included in either series if complications existed on admission. All cases in which serum was used were discarded from both groups. The prontylin-treated cases showed slightly less simple cervical adenitis of moderate degree, slightly more rhinitis, and more skin infections. Sinusitis occurred once under prontylin treatment and twice in the control group. Nephritis occurred once in the control group. On our first tabulation there was also one case among the prontylin-treated group, but this case was discarded because it was determined that the first mild symptoms of this nephritis were in evidence on admission. Among the prontylin-treated group six patients developed suppurative otitis media, while in the control group this occurred in fifteen cases. There were four cases of bilateral suppurative otitis media in the prontylin-treated group, and six among the controls. Thus out of the total thirty-one ears involved, ten were in the prontylin-treated group, and twenty-one in the controls. There was one unilateral surgical mastoiditis in the prontylin-treated group, and there were two in the controls. One case of bilateral surgical mastoiditis occurred in each group. Therefore, among the seven mastoids involved, three were in the prontylin-treated group and four were in the control group. There were no deaths. No prontylin rashes developed in this series. Vomiting was apparently caused by the drug in two cases. The blood picture was not disturbed. The results favor the prophylactic use of prontylin in scarlet fever, but they do not warrant undue enthusiasm. As far as otitis media is concerned, we were reminded that the first reports of serum-treated cases were misleading, and that one hundred cases of scarlet fever offer insufficient evidence. Apart from this series, the use of prontylin in five septic cases with positive blood cultures resulted in five recoveries. Only one of these belonged to the above series, and this one was among those originally treated with prontylin.

Academy News

The eighth annual meeting of the Academy will be held at Del Monte, Calif., on June 9, 10, and 11, 1938. This meeting will precede the annual meeting of the American Medical Association in San Francisco on June 13 to 17. This will be the last annual meeting to be held in the spring. It was decided at the last meeting of the Executive Board that future annual meetings will be held in the fall. The Section on Pediatrics of the American Medical Association will meet on June 15, 16, and 17.

Dr. Rieta C. Hough, San Diego, Calif., has been elected to membership in the Academy.

News and Notes

At a meeting of the **New York Academy of Medicine** on March 3, 1938, Dr. Béla Schick of New York City, was presented with the Academy Medal on the occasion of the twenty-fifth anniversary of the publication of his work on immunization in diphtheria.

The **American Pediatric Society** will hold its fiftieth annual meeting at the Berkshire Inn, Great Barrington, Mass., on May 5, 6, and 7, 1938. The **Society for Pediatric Research** will hold its tenth annual meeting at the same place on May 4 and 5, 1938.

Dr. Barnet E. Bonar, of Salt Lake City, was fatally injured in an accidental fall on the night of Dec. 19, 1937. Dr. Bonar has contributed critical reviews to this JOURNAL on conditions related to the newborn infant. His death is keenly felt by the editors of the JOURNAL and by the pediatric profession at large.

The **American Board of Pediatrics** will hold examinations in New York City on May 3 and in San Francisco on June 12. Information regarding examination may be obtained from Dr. C. A. Aldrich, secretary, 723 Elm Street, Winnetka, Ill.

Correspondence

London, England, February 11, 1938.

In my last letter comment was made upon the national campaign to improve physical fitness by means of physical education and training of young people. Since then, early in 1937, a governmental report on the matter has been published. An important point of policy is the decision that physical education should be upon a voluntary basis, and that nothing of the nature of a compulsory system should be introduced. The report states that the Government proposed to appoint two national advisory councils, one for England and Wales, and one for Scotland. The memorandum points out that research on both medical and physiological lines is required in regard to physical training, and it is of interest to the medical profession that such investigations of problems connected with physical education are envisaged. This governmental report was preceded in the previous year by a circular on the same subject, issued by the Board of Education. In the Board's report for 1936, recently published, great stress is laid upon this important aspect of national well-being.

In his annual report as Chief Medical Officer to the Board of Education, Sir Arthur MacNalty again discusses the nutritional state of the school child, a subject obviously of much interest to paediatricians, and one on which I have commented before. It appears that in many areas the physique of elementary school children, as measured by weight and height, has continued to improve. The figures taken as a whole, however, are almost identical with those of the previous year. Actually, during 1936 the nutrition of 1,726,755 children was assessed by 1,300 observers at routine medical inspections. Of these children 10.5 per cent were regarded as being slightly subnormal nutritionally, and 0.7 per cent as being in a nutritionally bad state. It is, of course, common knowledge that the personal factor involved in assessing nutrition is a dominant one, and in this connection a paper recently given by Mr. R. Huws Jones before the Royal Statistical Society is of considerable interest. His subject was "Physical Indices, and the Clinical Assessments of the Nutrition of School Children." In his inquiry into the subject, Mr. Jones was led to test medical officers themselves. Here he found, for instance, that one school medical officer examined 193 children, and at his first examination placed 36 in class A, 146 in class B, and 11 in class C, while a week later his grouping was 48 in A, 142 in B, and 3 in class C. It seems to be impossible, by a combination of measurements, to arrive at a really certain "index" of nutrition, which will replace the judgment of a trained observer, though obviously physical measurements must be employed by him. In the present state of knowledge the connotation of the term "malnutrition" is not precise enough for it to be possible to adopt routine methods which would permit of numerical results being reached which would be at ance strictly comparable and really informative for all parts of the country. Perhaps in examining children from the nutritional standpoint the wisest thing would be to mark down those children who need further medical supervision.

In the course of the past twelve months, the Advisory Committee on Nutrition, set up by the Government in 1935, have published their first report. The national diet appears to be deficient in certain "protective foods," eggs, green-leaf vegetables, and particularly milk, the average consumption of the last-named being only about one half of what it ought to be per head of the population. The inclusion in the diet of more potatoes is advocated, while it is agreed that less sugar, less white flour,

and more lightly milled cereals would be advantageous. All of the population, except a relatively small fraction, are obtaining the full number of calories that they require.

More especially on account of the efforts to increase the amount of milk consumed, it is of paramount importance that milk should be rendered safe; despite, however, the strong feeling within the medical profession in this country, already commented upon in my letter of May, 1934, opposition to pasteurization is still forcible. It is, however, good to know that in the forthcoming Milk Bill a measure of compulsory pasteurization is promised. So far as milk is concerned, the Board of Education not unnaturally advises pasteurization whenever possible.

Efforts to set up a standard of prematurity, based upon birth weight, are still proceeding, with a view to fixing a definite criterion upon which to base a statistical comparison of material. This is regarded as an important preliminary stage in any campaign to lower infantile mortality, because of the necessity for special consideration of immature infants. The matter has aroused the interest of the Royal College of Physicians, and there is reason to believe that it will take action calculated to assist in laying down such a standard.

The last meeting of the British Paediatric Association, held at Windermere, has already been reported in the medical press. A noteworthy feature was the opening of a discussion by Professor E. Gorter, of Holland, on nutritive food requirements during the first year of life, as set out in the League of Nations Memorandum of December 12, 1936; this stimulated a lively discussion. This year the meeting of this Association is to be held in May at St. Andrew's, under the presidency of Dr. J. Wilkie Scott, of Nottingham. It is the first time the Association has met in Scotland, and the choice of place is such as to make one confident that the golfing prospects may prove as great an attraction as the more serious part of the programme.

KENNETH H. TALLERMAN.

Book Reviews

Atlas of Skeletal Maturation (Hand). T. WINGATE TODD. St. Louis, 1937, The C. V. Mosby Company, pp. 203, price $7.50.

After a brief introduction to the study of the skeletal maturation, which has been the interest and work of Dr. Todd and his associates for a number of years, seventy-five large plates showing the maturation of the bones of the hand from infancy through adolescence are presented. Forty of these are male white hand standards and thirty-five, female. As skeletal maturation is perhaps the best criterion of "growth" which we possess, the importance of the Atlas is obvious. It will be found invaluable for furnishing standards for comparison for workers in the field of child development and pediatricians. It is well printed, and the individual plates have been carefully selected from the many thousands in Dr. Todd's laboratory.

The Compleat Pediatrician. W. C. DAVISON, Ed. 2, Durham, N. C., 1938, Duke University Press, price $3.75.

It is only occasionally that revised editions of an old book are given review space in the JOURNAL. This second edition of Dr. Davison's unusual manual published a few years ago is so completely revised, so bears out the statement "completely re-written," that it is in reality a new book. The new arrangement of material, the reduction in the numbering of paragraphs which made the first edition rather irritating to use, the inclusion of new material, as for example, the excellent chapter on Growth, Development and Guidance of Children have so improved the book that it is infinitely superior to the first edition, which it has in fact, rendered obsolete. It contains a veritable mine of information, and we know of no other single volume more useful for the pediatrician's desk. We prophesy an even more popular reception than that accorded to the first edition. It is easier in many ways to write a new book than completely to revise and rewrite an old one, and the author is to be congratulated on the unusual success of his efforts.